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THE CHICAGO MEDICAL SCHOOL
QUARTERLY

VOLUME 17 MAY 1956 NUMBER 3

SIMPLE SHUNTS

OLGA M. HARING, M.D.* and HERBERT D. TRACE, M.D.**

Introduction and History

It has become a custom in medical literature to begin the history of congenital heart disease from 1939, the year when the first successful surgery in a patient with patent ductus arteriosus was reported[1]. This was a powerful stimulus that awakened a more generalized interest in a large group of the medical and non-medical population all over the world, due to its implication that the diagnosis of congenital heart disease may offer a cure to the patient instead of resignation. Clinical interest in congenital heart disease and, knowledge of its pathophysiology, has been growing steadily since 1939. The number of patients who have, since then, been benefitted by surgical treatment is significant. The rapid advance of cardiac surgery has been furthered through the continuous efforts to improve the operative technique, use better anesthesia, and attain complete control of infection. A more rewarding challenge is, therefore, offered to the clinician to select the proper cases for surgery. Today, the diagnosis of most of the common types of congenital heart disease can be made on clinical grounds. To make this possible, facts and knowledge obtained through the life-time work of innumerable investigators during the past 150 years had to be gathered and integrated. This was done by cooperative efforts of the clinician, the physiologist, the pathologist and the surgeon.

Our knowledge of congenital heart disease started with observations made by the anatomist. Occasional autopsy findings of malformed hearts were considered by the anatomists of the eighteenth century as a curiosity of no clinical significance[2]. At the beginning of the nineteenth century, with Laennec's[3] discovery of the stethoscope, the era of modern physical diagnosis began. Acquired and congenital heart diseases were diagnosed at the bedside, and clinical and postmortem findings were correlated. While the clinicians described most of the common types of congenital heart disease known today with accurate observations[4,5,6,7], anatomists started investigations as to the cause and mechanism of cardiac malformations[9,8,10]. Meckel pointed out in 1812, that malformed human hearts commonly present a close similarity to the normal hearts in the lower vertebrate scale. At the beginning of our century, Abbott's[11] brilliant analysis of 1000 autopsied cases gave the first comprehensive study to the medical world. She not only offered the first useful classification of congenital heart diseases, but discussed "intracardiac surgery as a pos-

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sible means of curing or alleviating some of these conditions." She also mentioned Monro's suggestion to ligate a patent ductus arteriosus and referred to Carrell's and Tuffier's experimental work on attempts to enlarge a stenotic pulmonary valve[12].

New diagnostic methods such as roentgenology, electrocardiography and particularly the introduction of cardiac catheterization for physiologic tests, increased our knowledge in the abnormal hemodynamics produced by congenital malformations. Many a "bizarre symptomatology" described by Abbott has been, since then, analyzed and understood. Cardiac catheterization made it possible to determine oxygen saturations within the cardiac cavities, measure pressure in the various chambers and in the great vessels, determine pulmonary blood flow and pulmonary resistance and, lately, to introduce selectively radioopaque substances in the cardiac cavities to visualize septal defects and other malformations. Correlation of data obtained through cardiac catheterization and angiocardiography, with the simpler diagnostic methods such as electrocardiography, fluoroscopy and thorough physical examination, elucidated certain characteristic manifestations in the different types of malformations[13, 14, 15, 16]. These malformations can be recognized on clinical grounds by the internist and the pediatrician. The purpose of this paper is to give a brief and comprehensive presentation of the characteristic features of malformations causing simple cardiac shunts.

Definitions and Classification

Malformations within the heart or of the great vessels cause mechanical disturbances which interfere with normal cardiac function. The greater the disturbance, the earlier and more serious will be the repercussions. The cause of abnormal organogenesis is not known[17, 18]. For our purposes, it is sufficient to state that there is satisfactory evidence that structural malformations consist either in persistence of fetal communications between the different chambers of the heart or the great vessels, or in narrowing at some points of the cadiovascular tract. At the time of birth, arterial and venous blood flow are separated; the pumping load of the right and left ventricle is balanced. If, however, the cardiac septation is defective, or if any of the fetal cardiovascular passages persists, a detour of the blood flow from its normal route will result. The direction of the flow through the abnormal communication will be from the left chambers into the right chambers, and from the aorta into the pulmonary artery, because the pressure is usually higher on the left side of the heart than on the right. In these cases, we say that there is an arterio-venous shunt. All arteriovenous shunts, which are not accompanied by other pathological functions of the cardiovascular system, are *Simple Shunts*. A second group of abnormal hemodynamics results from *Obstructed Flows*, caused by narrow passages. The third results from a combination of both conditions, and we call these *Composite Shunts*.

A review of the clinicopathological syndrome of the Obstructed Flows and Composite Shunts will be the subject of another communication.

SIMPLE SHUNTS

The common feature of every left-to-right shunt is an increased blood flow in the pulmonary circulation and a corresponding decrease in the systemic circulation. These hemodynamic changes may or may not be significant depending upon: 1) the extent to which they disturb the right-to-left balance of the cardiac pumping load; 2) the interference with the oxygenation of the blood; and 3) the decrease in oxygenated blood volume to the systemic circulation. The fate of any patient with a left-to-right shunt depends on the following factors: 1) the size of the passage for the shunt; 2) the chamber into which the shunt occurs; 3) the adjustment pattern of the pulmonary vascular bed to increased flow or the predisposition to pulmonary hypertension; and, 4) the specific complications due to rheumatic fever and subacute bacterial endocarditis.

Simple shunts can be divided into 3 groups: (A) Shunts occurring into the

TABLE 1.

Clinical and Hemodynamic Features of Simple Shunts

	Atrial Septal Defects	Ventricular Septal Defects	Patent Ductus Arteriosus
ECG	R.V.H.	C.V.H. or R.V.H.	L.V.H. or C.V.H.
X-Rays	R.A. and P.A. enlarged. Periph. vasc. markings increased.	R.V. and P.A. enlarged Periph. vasc. markings increased	L.V. and P.A. enlarged Periph. vasc. markings increased.
Cardiac cathet. data.	Pressure in R.V. and P.A. normal 0_2 saturation of blood increased in R.A.	Pressure in R.V. and P.A. increased 0_2 saturation of blood increased in R.V.	Pressure in R.V. and P.A. normal or slightly increased 0_2 saturation of blood increased in P.A.
Clinical course	Right ventricular failure	Pulmonary hypertension Right ventricular failure	Moderate pulmonary hypertension Left or combined heart failure
Life expectancy	30-40 years	30-40 years	30-50 years
Treatment	1. Surgery (15-25% mortality) in shunts twice larger than systemic flow 2. Prevention of heart failure	1. Prevention of heart failure and SBE Surgery is still in experimental stage	Surgery (0.5—2% mortality)

right atrium; (B) Shunts occurring into the right ventricle; (C) Shunts occuring into the pulmonary artery. (Table 1)

A. Shunts into the Right Atrium

In shunts into the right atrium, fully oxygenated blood is shunted from the left atrium through defects in the septum (atrial septal defects); or from the lungs via anomalous connections of the pulmonary veins (anomalous drainage of pulmonary veins).

Atrial septal defects

Openings in the atrial septum are due to partial or complete absence of the septum primum, the septum secundum or a combination of both. A so-called patent foramen ovale must be distinguished from an atrial septal defect, since the former never permits a left-to-right shunt. However, a right-to-left shunt is possible if the pressure in the pulmonary artery and right ventricle rises significantly, and an incompetent tricuspid valve transmits the high pressure to the right atrium.

Hemodynamics

If a significant amount of arterial blood is shunted into the right atrium, it is thus added to the normal intake of the right ventricle which will then increase its output correspondingly. The consequences are hypertrophy and dilatation of the right atrium and of the right ventricle, and dilatation of the pulmonary artery. Progressive right ventricular enlargement eventually leads to right ventricular failure. At this point, the pressure rises in the right atrium and, if it exceeds that in the left, the shunt is reversed and cyanosis may appear. The pressure in the pulmonary artery usually remains normal, despite a pulmonary flow of two to three times the systemic flow[19,20]. In these cases, apparently, the diastolic filling of the right ventricle limits the amount of blood which can be shunted from the left, and thus protects the pulmonary circulation from overloading.

Clinical features

The clinical features vary with the size and location of the defect. With small defects there are no symptoms. With medium-sized defects, there may be no symptoms until the third or fourth decade. At this time, right ventricular

enlargement has progressed to a significant degree and eventually leads to right ventricular failure. Associated with the failure, cyanosis may suddenly appear. Arrhythmias of atrial origin are frequent and are probably due to dilatation of the atria. Patients having a very large defect may have exertional dyspnea and increased fatigability at an early age. They are underdeveloped and thin. These manifestations can be explained by the decreased left ventricular output and the diminished peripheral circulation. Physical findings include a basal systolic murmur, usually maximal in the second and third left intercostal spaces, and a prolonged second pulmonic sound. Fluoroscopy reveals dilatation of the pulmony artery, increased hilar and peripheral vascularization of the lungs, and enlargement of the right atrium and right ventricle. Typical electrocardiographic findings are partial or complete right bundle branch block and right atrial hypertrophy. Cardiac catheterization confirms the diagnosis by demonstrating the increased oxygen saturation of blood samples obtained from the right atrium as compared with samples of vena caval blood.

The prognosis in small defects is good, while patients with significant shunts usually die, in congestive heart failure, before the sixth decade. Complications may further reduce their allotted life span. Rheumatic fever is not uncommon in patients with septal defects and, if the sequella be mitral stenosis, an additional burden is placed on the right ventricle. Pulmonary hypertension occurs in certain cases in very young children, or in other patients later in life.

Treatment

Surgical repair of atrial septal defects has been successfully performed in several centers in this country since 1952[21,22]. The techniques vary with the location and size of the defect. Lesions of moderate size, located posteriorly in the septum, are best suited for external suture repair. Large, multiple, or low defects have been approached under direct vision with the aid of hypothermia[23,24]. Successful closure has been effected in a number of cases as shown by postoperative cardiac catheterization. The shunt was completely obliterated after surgery and, in those patients where pulmonary hypertension was present before, a decrease in the pressure of the pulmonary artery was noted.

The all-over mortality in repair of atrial defects is 15-20%. Therefore, it should *not* be recommended as a routine operation. Surgery should be advised *only* for patients with a history of congestive failure, a marked exercise limitation, and a shunt at least two times greater than the systemic flow[25]. Pulmonary hypertension and marked cardiac enlargement are not contraindications, as these conditions are usually benefited by surgical closure of the defect. It is anticipated that with increasing experience the mortality of the procedure will progressively decrease. With a decrease in the mortality, the criteria for our present selection will be altered.

If surgery is not considered, medical treatment should be directed toward the prevention of congestive failure.

Anomalous drainage of pulmonary veins

Complete anomalcus drainage of both lungs into the right atrium is a severe malformation, and death occurs before one year of age.

Partial anomalous drainage, if it is an isolated malformation, has no clinical significance. Not infrequently, they are combined with atrial septal defects. Hemodynamics and clinical features are similar to those described in atrial septal defects. Diagnosis is not easy in these cases, and can be best made by dye visualization techniques. Repair of anomalous veins is usually done in cases where surgery for atrial septal defect is performed[26,27,28].

B. Shunts into the Right Ventricle

Ventricular septal defect

These occur from the left ventricle through defects in the membraneous or the muscular portion of the interventricular septum.

Hemodynamics

The larger the defect, the more signifi-

cant the hemodynamic repercussions will be[29, 30, 31, 32, 33].

Large defects. If the area of the defect approximates the cross-sectional area of the aortic orifice, the systolic pressure in both ventricles, the aorta and the pulmonay artery are equal; and a common ejectile force is shared. Consequently, the distribution of blood into the two circulations is dependent on their respective peripheral resistances. If the pulmonary resistance is low, the larger amount of blood will pass, with each ejection, to the lungs and not to the body. In order to maintain adequate systemic flow, the cardiac output rises and, eventually, a high output failure will result. If the pulmonary resistance is moderately increased, a certain balance between the two circulations is established, and there may, at least temporarily be, no flow through the defect. If the pulmonary resistance is high and increases progressively, it may eventually exceed the systemic resistance. Cyanosis, anoxia and right ventricular failure are the ultimate consequence.

Medium sized defects. If the defect is not larger than one third of the aortic orifice, the pulmonary flow varies in proportion to the resistance in its vascular bed. Usually, there is a slow progression of the pulmonary hypertension with progressive right ventricular enlargement and failure.

Small defects. Small defects in the muscular portion of the septum cause minimal shunts. The reason for this is that during systole, when most shunting ordinarily occurs, the size of the defect is decreased by the septal and ventricular contraction.

Clinical features

Symptoms may be completely absent if the shunt is small and then the lesion is discovered only accidentally. With larger shunts, manifestations due to decreased systemic flow may appear. Cyanosis and congestive failure occur in patients with marked pulmonary hypertension. The most important physical finding is a loud systolic murmur, frequently accompanied by a thrill, maximal at the left sternal border in the third and fourth intercostal spaces. Fluoroscopy shows, as in atrial septal defect, a dilated pulmonary artery. However, the peripheral vascularization of the lungs is not always increased. Moderate enlargement of the left, or both ventricles, may also be present. The electrocardiogram can be normal, or can show left or combined ventricular hypertrophy[34]. Cardiac catheterization establishes the diagnosis on the basis of blood gas analysis. It also gives a conception of the severity of the disease by establishing the pressure conditions, the pulmonary resistance, and the right ventricular work[35, 36, 37]. The prognosis in patients with relatively small shunts is good, if complications can be prevented. Subacute bacterial endocarditis is a frequent cause of premature death. In larger defects, the prognosis is more serious. In extremely severe cases, death may occur in the first six months of life. Occasionally, however, infants with large septal defects and congestive failure may improve after the first year. A possible explanation for this fact is that, as the child and his heart grows, there is a relative decrease of the size of the defect.

Treatment

In the last few years, Dammann proposed palliative surgical treatment in order to control the excessive pulmonary blood flow. By surgical creation of a pulmonic stenosis, the cardiac load may be decreased and the patient's life prolonged. In a small number of cases with very large shunts and markedly dilated pulmonary arteries, satisfactory results were obtained. Complete closure of the septal defect under direct vision, by means of controlled cross circulation, has been recently reported. These methods are still in the experimental stage[38, 39, 40]. Medical treatment particularly in mild cases, should be mainly concerned with the cure and prevention of congestive failure and infection.

C. Shunts into the Pulmonary Artery

Shunts of oxygenated blood into the pulmonary artery come from the aorta by means of a patent ductus or, in rare cases, through an aorto-pulmonary septal defect or a ruptured aneurysm of the sinus of Valsalva.

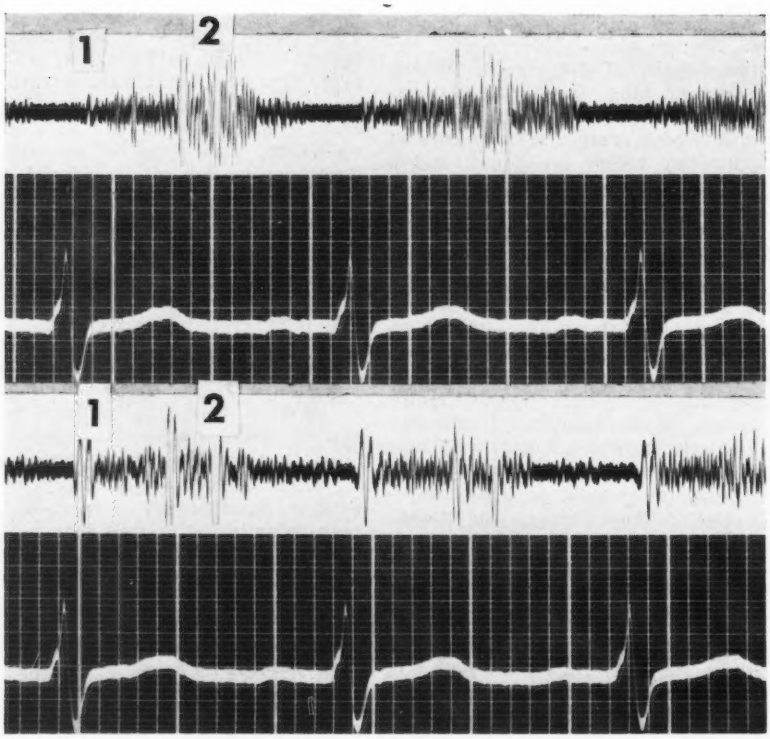

Fig. 1. Phonocardiogram showing typical late systolic, early diastolic murmur in cases of uncomplicated patent ductus arteriosus.

Patent ductus arteriosus

The ductus arteriosus is a fetal vascular communication between the aorta and the pulmonary artery. The direction of the blood flow, the pressure being higher in the right than in the left ventricle, is from the pulmonary artery into the aorta. After birth, the ductus loses its physiological function and closes completely before the end of the first year in ninety-nine per cent of the cases. The mechanism of persistent patency or delayed closure has not, as yet, been explained satisfactorily.[41, 42, 43, 44]

Hemodynamics

In typical cases of patent ductus, there is a continuous flow of blood from the aorta into the pulmonary artery. If the ductus is wide, the shunt is large, causing an increased volume of blood to pass through the lungs, the left atrium and the left ventricle. The increased pumping load requires increased left ventricular work, and leads to left ventricular hypertrophy. In a certain number of cases, the large pulmonary flow is met by a progressive increase in resistance to the flow, and a pulmonary hypertension develops. Eventually, the direction of the flow may be reversed and cyanosis then appears. In the third group of patients, soon after birth, a progressive left ventricular failure develops leading to death, unless surgical closure of the ductus is performed. We assume that the cause may be due to the fact that, during fetal life, the left atrium and the left ventricle must have suffered such developmental handicaps that, at the cessa-

tion of fetal circulation, these chambers were not adequately prepared to receive the load of blood from the lungs and pump it into the systemic circulation[44].

Clinical features

The great majority of patients have no symptoms[45, 46]. Some may show evidence of exertional dyspnea, easy fatigability and stunted growth. Physical examination is usually sufficient to make the diagnosis. The classical "continuous" or "machinery-type" murmur is best heard in the second interspace to the left of the sternum, and is accompanied by a thrill. If the murmur is not continuous through entire systole and diastole, a phonocardiogram is useful showing the typical late-systolic, early-diastolic murmur in cases of uncomplicated ductus[47] (Fig. 1). On fluoroscopic examination, the pulmonary artery is usually dilated, shows increased pulsations, and the vascular markings of the lungs are also increased. The left ventricle is usually enlarged. Cardiac catheterization is necessary in doubtful cases. Visualization with dye can also be helpful, but a definite diagnosis can sometimes only be made by exploratory thoracotomy. The prognosis in very mild cases is good but, even in these cases, surgical treatment should be advised, for the danger of the most frequent complication, subacute bacterial endocarditis, is present in twenty per cent of the cases treated non-surgically.

Treatment

The surgical method of choice is complete division of the ductus. The results are excellent and surgical mortality is minimal (two per cent). The presence of pulmonary hypertension is not a contraindicating factor as long as an aorto-pulmonary shunt is still demonstrable. Frequently, pulmonary hypertension is reversible if the patient is operated at an early period, where no degenerative changes of the intima of the pulmonary vessels have taken place. The results of surgery in patent ductus, with reversal of flow, are poor[48, 49, 50]. With the exception of the early malignant types of ductus, where surgery is life saving, the optimum age for the intervention is between eight to ten years.

Aorto-pulmonic septal defect

This is rare as an isolated malformation. The differential diagnosis from patent ductus is difficult, and there is no satisfactory treament for this condition, although successful surgical repair has been reported.

Summary

Aberrations from the normal developmental pattern of the heart and of the great vessels modify progressively the postnatal circulation. Each type of structural defect induces specific hemodynamic alterations. Classification of congenital heart disease proposed by previous authors is not satisfactory at the present state of our knowledge. A new classification is proposed in this paper, based on the anatomical defects with implication of the pathological repercussions.

Congenital malformations can be divided into three groups, in those causing:

(1) *Simple Shunts,* due to persistance of fetal communications between the different chambers of the heart and of the great vessels; in those causing

(2) *Obstructed Flows,* due to narrowed passages, and in those causing

(3) *Composite Shunts,* resultant of combination of narrowed passages with persistent fetal communications between the heart and the great vessels.

The characteristic hemodynamic alterations, the clinical features, and the treatment in Simple Shunts are reviewed. The significance of early and accurate diagnosis is stressed to determine the optimal time for elective surgery in lesions in which operation can offer improvement or cure. For defects, which at this time are not amenable to surgery, prevention of heart failure and of infections are recommended with the hope that ultimate cure will be possible in the near future.

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JAUNDICE

ALEXANDER B. WHITE, M.D.*

Bilirubin is an iron free product of hemoglobin. Its major source is the hemoglobin of the broken down mature erythrocytes, although a small part of the bilirubin is derived by synthesis from porphyrin precursors or/and from the broken down fraction of hemoglobin originating in the early stages of erythrocyte maturation.

The porphyrin ring of the hemoglobin is opened (probably by the way of an oxidative mechanism) by removal of the alpha methene bridge between ring I and II, yielding verdohemoglobin. The iron, which within the hemoglobin molecule is tightly bound, is only loosely connected in the verdohemoglobin and thus easily removed, yielding bilirubin. It is assumed that the bilirubin thus formed remains attached to the original globin of the hemoglobin molecule and is called "indirect reacting" or bilirubinglobin. The attachment is believed to be by carboxyl groups as in the original hemoglobin!

This formation of bilirubin takes place in the reticuloendothelial system. The bone marrow plays a major role in its formation, the spleen to a lesser degree, and the Kupfer cells have a relatively minor role. The polygonal liver cells, *per se*, have no function in the formation except excretion of the bilirubin.

The bilirubinglobin is carried by the blood stream into the liver where it is divested of its protein (globin) by the Kupfer cells and probably also the polygonal cells and is excreted into the bile, probably in the form of its sodium salt as sodium bilirubinate (also called the "direct reacting" bilirubin.) This direct reacting bilirubin may pass in the urine if it circulates in the blood and as a matter of fact, even before jaundice may be evident. The indirect reacting bilirubin doesn't pass in the urine.

This theory on the two types of bilirubin has been challenged by many authors. They believe that there may just be one type of bilirubin which acts differently under different circumstances at different rates of speed. It is believed by some authors that both bilirubins are bound to protein, but that the "indirect reacting" is more firmly attached. The kidney is somehow able to release it from its bond[2,3]. From the practical standpoint, however, the original theory of the two types of bilirubin seems to be useful in offering an adequate understanding of the pathophysiology in the differential diagnosis of jaundice. Recently also, some additional supportive evidence of this old theory has been offered by crystalization and chromatographic studies. Lathe by chromatographic studies describes three forms of bilirubin, one indirect and two types of direct bilirubin. The latter are both metabolites of bilirubin and the liver plays an essential role in their formation. Hoffman and Bollman[4], however, have done similar work and concluded also that two types of direct reacting bilirubin are present in jaundiced patients, and that the diazo reaction is dependent on the nature of the pigment and not the attachment of the protein molecule. The serum in hemolytic jaundce shows only the indirect reacting pigment with small amounts of direct pigment I and II; in hepatocellular jaundice, pigment I predominantly, and in obstructive jaundice, mainly pigment II. The trace of "direct reacting" bilirubin which normally may be found in the serum may be related to the variations in the flow of bile. During slowing down of the metabolic activities, as in sleep, a relative degree of bile stasis occurs with resulting minimal regurgitation, either through increased permeability of bile capillaries or otherwise[5].

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TYPES OF JAUNDICE

Prehepatic | **Hepatic** | **Extrahepatic**

Intralobular

1. As in constitutional hyperbilirubinemia.
2. Retention jaundice due to subnormal liver function.
3. Regurgitation jaundice due to hepatocellular necrosis, cholangiolitis, bile-lymph reflux.

Extralobular

Regurgitation jaundice as in cholangitis, regurgitation due to canalicular bile-lymph reflux, and due to disruption of hepatocellular-canalicular continuity.

The Enterohepatic Circulation of Bilirubin

After passage of bilirubin into the biliary passages, it becomes first oxidized to biliverdin, then under the influence of bacteria in the intestine is reduced to mesobilirubinogen and stercobilinogen, both designated as urobilinogen and giving the Ehrlich aldehyde reaction. The greater part is thus excreted in the stool.

A small part of this urobilinogen is reabsorbed and carried via the portal circulation to the liver where it is retransformed into bilirubin, of which a part again remains in the circulation and appears in the urine. In infections within the biliary tree, urobilinogen may be formed before entering the intestine, which possibly accounts for the occasional appearance of urobilinogen in the urine in the extrahepatic obstructive jaundice, and bile fistulas. In some of these cases the urobilinogen may be due to absorption of pigment from desquamated cells within the gastrointestinal tract which show biliary pigment inhibition. Suppression of the intestinal flora, for example, as with wide spectrum antibiotics, or rapid passage of bowel contents as in diarrhia, also influences the formation of urobilinogen. In the case of antibiotics, however, there is a return to the previous state after a few days of antibiotic therapy.

This exclusively enterogenous theory has been challenged by Baumgertel, who offers an additional hepatogenous theory.

The other constituents of bile are not of great importance in this discussion, and will be omitted. It should be mentioned, however, that the bile salts are formed in the liver and also pass through an enterohepatic circulation.

Classification of and the Pathogenetic Mechanism of Jaundice

Any interference with the normal metabolic or excretory process of bile pigment will result in jaundice. Many different classifications of jaundice have been proposed. The most suitable for our discussion here is the one taking into consideration the pathogenetic mechanism involved. Such has been proposed by McNee and later modified by Lichman[6]. It must be understood, however, that any classification is far from ideal due to the fact that a pure type of jaundice is very rare and in each case a number of pathogenetic factors is usually involved. This fact is also one of the responsible causes of the difficulties encountered in the diagnosis of the types of jaundice with the presently available laboratory methods.

Prehepatic Jaundice (Hemolytic or Overproduction Jaundice)

This type of jaundice is due to over-

productiton beyond the handling capacity of the liver.

Overproduction alone, as the cause of this type of jaundice has been denied by Rich and other investigators. The reason for this doubt lies in the fact that the liver which is known for its marked functional reserve even in the absence of three-fourths of its mass, should be able to handle the overproduced bilirubin. It is believed, therefore, that additional impairment of liver cell function caused by factors associated with hemolysis, play an additional although lesser role. Among these factors are: a.) the developing anemia with resulting anoxemia of the liver, b.) fever and toxicity so frequently associated with hemolysis, c.) circulatory disturbances, d.) the basic underlying disease, like lymphomas, dyscrasias, malignancies, etc., and others. Later in the disease, when marked involvement of the liver has occurred, or an additional obstructive factor (for example, pigment stones) has entered the clinical picture, the latter mechanisms may then predominate. As long as excessive formation remains the primary factor of the jaundice, the bilirubin in the serum will be of the indirect type, and no bile will appear in the urine (acholuria). The urine and fecal urobilinogen will, however, be increased due to the increased amounts of bilirubin delivered into the biliary passages. In neonatal icterus, immaturity of the liver cells, and also a direct blood-lymph bilirubin shunt have been shown to play an additional role besides overproduction.

Hepatic Jaundice (Hepatocellular Retention Jaundice without Impairment of Bile Flow)

This type of jaundice would occur in cases where: 1.) An increase in the threshold for the passage of bilirubin from the liver cell into the billiary canaliculi is present. 2.) Production beyond the capacity of handling it by the liver cell due to mainly over-production (has already been discussed above), or disturbance of the liver parenchyma to such a degree that it is unable to handle the normally produced amounts of bilirubin.

The example for the first type is the so-called constitutional hyperbilirubinemia (familial non-hemolytic jaundice, icterus intermittens juvenilis, cholemie simple, Gilbert's disease). In this condidition there is an elevation of the serum bilirubin found, without histological evidence of liver cell damage. No impairment of liver cell function is detectable here, except for this abnormal excretion of bilirubin. BSP is excreted in a normal manner. Studies for detection of a possible silent hemolysis being the cause for the hyperbilirubinemia has yielded negative results. A selective dysfunction in the excretory threshold for bilirubin is believed to be responsible for this conditon. The suggested explanation for this increased threshold includes: a possible abnormality of the size of the bilirubin particles, or an increase in the permeability of the Kupfer cells, so that a higher blood level is necessary to activate the excretion mechanism.

The bilirubin is of the indirect type in these cases, and there is acholuria. It is essentially an asymptomatic, benign condition, and the fatigue with asthenia occasionally complained of by these patients is believed to be of iatrogenic origin.

Hult has suggested the possibility of this not being a separate entity, but a posthepatitic state, after all the clinical and functional manifestations of the original disease have subsided. A few cases where there is a mild elevation also of the direct bilirubin but classified under the constitutional hyperbilirubinemias might possibly belong to this latter posthepatitic category.

At this point I would like to mention the so-called Dubin-Johnson syndrome, or chronic idiopathic jaundice with an unknown pigment in the liver which has been recently separated from the constitutional hyperbilirubinemias[7,8]. This is a condition characterized by recurrent jaundice exacerbated by infections, surgical procedures and other stresses. The direct bilirubin is here increased in

contrast to constitutional hyperbilirubinemia. The liver function tests are essentially within normal limits except for the excretion of dyes which is impaired, such as the BSP test, and the failure to visualize the gall bladder with the Graham-Cole technique or other dyes. Cellular infiltration or bile stasis is absent, the only histological abnormality being deposition of an iron free unknown pigment within the liver cells. The authors suggest that an inborn deficiency of the liver cells exists being unable to properly excrete substances like BSP, dyes and bilirubin, including the unknown pigment. The pathogenetic mechanism as well as the nature of this pigment is, however, unknown yet, and must wait further investigation.

Other forms of mild latent jaundice with hyperbilirubinemia where none or minimal histologic changes are seen, as for example those associated with gastrointestinal diseases, etc., also belong to this category of hepatic jaundice (hepatocellular retention type). The typical cases of hepatitis, however, belong to the regurgitation type. Jaundice associated with pulmonary pneumococcal infections is also on a hepatocellular basis rather than hemolysis as shown by Zimmerman. The same may be true, at least to a degree, of pulmonary infarction since the liver is so sensitive to anoxia. The mechanism in congestive failure is very similar.

Hepatic Jaundice (Regurgitation Type with or without Impairment of Flow)

Under this heading belong all cases of jaundice in hepatitis (except the one mentioned above), cirrhosis and other affections of the liver where liver cell necrosis is evident, including the cases of intrahepatic billiary obstruction of intrahepatic-bile stasis without evidence of extrahepatic obstruction.

A number of factors can be enumerated here as being responsible for the bile regurgitation which may take place either via the lymphatics or directly into the blood. The predominant mechanism will be different in each individual case depending on the pathologic picture.

a.) Swelling of the liver cords may cause compression of the fine bile channels leading to regurgitation. That swelling can interfere with the bile flow has been best demonstrated in experiments with dogs. The latter when fed large amounts of glucose over longer periods of time, develop excessive accumulation of glycogen with swelling of liver cells and occlusion of bile channels with resulting regurgitation of bile.

b.) Bile thrombi (Eppinger) within the canaliculi or bile thrombi at the capillo-canalicular junction (caroli) as demonstrated by a special technic.

c.) Mechanical compression by regenerating nodules or granulomata, for example, as seen in sarcoidosis. An increased content of alkaline phosphatase in the vascular endothelium adjacent to such granulomata has been found by Shay[9]. It may be mentioned here that the rare occurrence of jaundice in sarcoidosis may be also due to parenchymal involvement (Shay), or a picture resembling cholangitic cirrhosis (Ross and Weinberg[01]), and extrahepatic obstruction.

d.) Interruption of bile channel continuity during nodular regeneration may also cause stasis until continuity is established.

e.) A block in the transmission of bile between the liver cells and bile capillaries and possibly also a liver cell—Kupfer cell block.

f.) In the presence of liver cell necrosis, the sodium bilirubinate may regurgitate through the space of the necrotic liver cells into the tissue spaces and then via lymphatics into the blood.

g.) Dissociation of liver cell columns may also cause obstruction of that unit.

h.) Portal triaditis with encroachment upon the ampullae joining the bile

capillaries with the small bile ducts. This, in addition to the mentioned bile thrombi and plugs and swelling of liver cell cords, has been suggested as the probable mechanism of jaundice in the intrahepatic billiary obstruction as described by Steigmann and Popper[11].

i.) Increased permeability of the cholangioles as suggested by Watson and Hofbauer[12] in their study in prolonged cases of hepatitis. In these cases relatively little evidence is present of reduced hepatocellular function, and the clinical picture suggests intrahepatic billiary obstruction. This increase in permeability and "dipedesis" of bile is believed to take place in those "vulnerable" ampullae which join the bile capillaries with the small ducts and then finds its way via the lymphatics into the blood stream. (One could speculate here that the beneficial action of cortisone or ACTH in hepatitis might possibly at least to a part be due to its action on this permeability. (This has also been recently suggested by other authors, who also suggest this procedure for a differential test.)

This would be consistent with the high rate of relapses on this type of management). Periportal cell accumulation, bile thrombi or increase in the liver cell cords was in some of Watson's cases absent to account for the obstruction. Minkowski and Naunyn also speculated on the possibility of direct excretion of bile constituents by the liver cells into the tissues spaces instead of bile capillaries.

j.) In the cases of intrahepatic bile stasis (Thorazine, testosterone, arsphenamine, PAS, etc.) it has originally been suggested by Hanger and Gutman[13,14] that an injury to the cell results in a disturbance of normal hydration of the bile which becomes too viscous to flow through the intralobular duct system. Here, also, no cell derangement, portal triaditis, or swelling is present in contrast to intrahepatic cholangiolitic obstruction to account for the jaundice. Increased permeability is the only explanation offered at the present time.

Extrahepatic Jaundice

The pathogenetic mechanism in frank extrahepatic obstruction appears quite apparent. Retrograde increase in pressure within the biliary tree occurs, which is followed by dilatation. When the pressure reaches above a critical level, rupture first of the "vulnerable" ampullae takes place. (The ampullae are considered by Aschoff as "fuses" protecting the liver cells and thus reducing the pressure.) The bile thus regurgitates either via the lymphatics into the blood stream or less often directly into the sinusoids. Studies in dogs after ligation of the common duct have shown a prompt appearance of bilirubin in the thoracic lymph duct. It probably is so that with lower pressures the way is via the lymphatics, whereas with higher pressures the direct way may be taken. It has also been noted that in normal livers the secretion granules within the liver cell localize toward the bile canaliculi; in other words in the direction of normal excretion, whereas in biliary stasis those granules often accumulate at the site facing the sinusoids suggesting possibly a change of the direction of excretion.

Increased permeability of bile capillaries, stasis, and secondary cholangitis probably also play a role, and later in the process of obstruction, additional liver damage occurs with all its consequences. That other factors, besides the reflux into the lymphatics, have to be considered in the pathogenetic mechanism of extrahepatic obstruction was well demonstrated by the studies of Grafflin and Chaney[15]. In mice with ligated common ducts, the authors have made direct observations of the liver during the excretion of fluorescent substances. They noted no dilatation or reflux into the lymphatics; however, shortly after the obstruction was produced, the hepatic cells have been noted to fail to take up the dye and little was excreted into the bile canaliculi.

MacLagan and Ducci[16,17] have investigated the presence of normal liver function tests in posthepatic jaundice. They were able to demonstrate that the serum of patients with posthepatic jaundice possesses a reduced tendency to flocculation and, therefore, the normal flocculation tests cannot be taken as evidence of normal function in these cases. This variability of factors explains the exceptional cases where marked obstruction may be present without the appearance of jaundice.

The bilirubin here is of the direct type and bilirubin appears in the urine. The amount of bile pigment in the stool, the degree of elevation of the alkaline phosphatase, the result of the flocculation tests, etc., all depend on the degree of obstruction and cellular dysfunction. Complete obstruction, for example, is uncommon with a stone obstruction as contrasted to cancerous obstruction. The hue of the jaundice, the time of appearance, presence or absence of pruritus also seem related to these factors.

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EXTRA-HEPATIC OBSTRUCTIVE JAUNDICE

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It has often occurred to this writer that many disease entities or syndromes, obstructive jaundice among them, can well be presented from the viewpoint of incidence according to age groups or physiological phases in the life of the human organism. A compelling reason for such a classification is the fact that differing etiological factors and susceptibilities are operative during these various phases. For example, the etiological factors in obstructive jaundice in early infancy are entirely different from those in other age groups; yet, the laboratory and clinical findings associated with this entity do not differ materially from those in other age groups.

Non-traumatic, extra-hepatic obstructive jaundice rarely occurs in individuals under the age of thirty. Almost the only exceptions are the occasional cases in early infancy. Even common duct stones as a cause is rather uncommon in this age group. In the writer's experience, the latter syndrome, even in persons who have had gall bladder stones for many years, rarely evidences itself much before the age of forty. In this age group, *e.g.*, infants to about age forty, the most common cause of extra-hepatic obstructive jaundice is traumatic stricture of the common duct following cholecystectomy. Obstructive jaundice due to carcinoma of the head of the pancreas, of the ampulla of Vater, or of the extra-hepatic bile ducts are entities that occur in persons of fifty or over, the highest incidence in persons of fifty-five to sixty-five.

While the subject of this paper is extra-hepatic obstructive jaundice, a short discussion of other types may aid in clarification. There are basically three types of jaundice; hemolytic, hepatocellular, and obstructive.

The most familiar form of hemolytic jaundice is the clinical form known as familial or congenital hemolytic jaundice. However, this disease entity may also be caused or associated with many poisons (snake venoms, vegetable poisons, *etc.*, chemical agents (trinitrotoluene, benzol, phenol, lead, *etc.*), bacterial toxins (Bacillus welchii, Streptococcus viridens, or hemolyticus), or certain disease entities, like Cooley's anemia, sickle-cell anemia, *etc.* The basic pathogenesis is the fact that many more erythrocytes are destroyed than can be properiy re-excreted as bilirubin by the liver cells, resulting in an excess of bilirubin in the blood. Normally, about 2,500,000 erythrocytes are destroyed or phagocytosed by the reticulo-endothelial cells per second.

The spleen contains the greatest concentration of these cells. When either because of increased phagocytic activity of the reticulo-endothelial (as in familial hemolytic jaundice) or because of exogenous poisons or toxins, more than the normal number of erythrocytes are destroyed per unit of time, the liver cells are unable to re-exrete bilirubin into the bile ducts and this product, therefore, appears in the blood in excessive concentration.

The symptoms of the common form of hemolytic jaundice — familial hemolytic jaundice — may first evidence itself early in life, or even in infancy. Usually, there is a familial history. The jaundice is ordinarily mild, but may become more marked during a "hemolytic crisis." There is splenomegaly (two to three times normal size), and mild to moderate anemia. The anemia, as well as the jaundice may become more marked during a "crisis" when more than an ordinary number of erythrocytes are being destroyed. The characteristic laboratory findings are microcytosis, anemia, increased red cell fragility, reticulocytosis (ten to twenty per cent) increased serum bilirubin (indirect), and increased urinary urobilinogen.

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Splenectomy, as the pathogenisis of this disease would suggest, results in cure in the overwhelming majority of cases. There are several features of this disease that are of special interest to the surgeon. The first is the fact that many of these patients, even as children, have associated gallstones. It is in this disease that pure bilirubin stones may be found. The patient may, therefore, present himself at first complaining of gall bladder colic. I shall cite a case in point later on.

The second is that because the rate of destruction of erythrocytes is greatest during the "hemolytic crisis," blood transfusions during splenectomy, particularly when done during such a phase, should not be started until after the splenic pedicle has been ligated, or, at least until the splenic artery has been clamped or ligated. This precaution also is valid in splenectomy for idiopathic thromboycytopenic purpura where the reticulo-endothelial cells destroy excessive numbers of platelets instead of erythrocytes. A case of this disease that I encountered eight years ago illustrates the above features and other situations that the surgeon may encounter.

The patient, a forty-one year old white female, presented herself for examination eight years ago. She had been studied elsewhere and the diagnosis of cholelithiasis made on a basis of a typical history of gall bladder colic for the past eighteen months and the finding of calculi on cholecystography. However, no roentgenographic studies were made of the upper gastrointestinal tract. These were ordered and, while the stomach and duodenum were found to be normal, a large splenic shadow was noted on the films.

The patient was hospitalized, and on examination, the lower edge of the spleen was palpated when the patient was in the sitting position. The red blood cell count was 3,400,000; the icterus index was thirteen; there was no increased red cell fragility, and the reticulocyte count was fifteen per cent. It was difficut to discern a definite icteric tinge of the skin or sclera. A diagnosis of familial hemolytic jaundice was made and a splenectomy performed. Blood transfusion was started after the splenic pedicle was ligated, since it was felt that because of the low erythrocyte count the patient was in a mild hemolytic crisis.

Following surgery, the patient's skin became much fairer and the laboratory findings returned to normal. On further questioning prior to surgery, the patient stated that her father had also been thought to be slightly icteric most of his life.

Cholecystectomy was performed ten weeks later. Several bilirubin stones were found in the gall bladder. It was felt that were cholecystectomy performed prior to the diagnosis of familial hemolytic jaundice, the trauma of this operation might have precipitated a serious hemolytic crisis.

Hepatocellular jaundice is the form most common in youth and early adulthood. While one of its forms, "catarrhal jaundice," is the most common, it may be associated with or caused by various infections (viruses, leptospiral infections, infectious mononucleosis, malaria, *etc.*), or poisons (arsphenamine, cinophen, chloroform, avertin, inorganic compounds of lead, bismuth, or arsenic poisonous mushrooms, snake venoms, *etc.*)

Catarrhal jaundice (infectious hepatitis) occurs, as a rule, in young people, and is usually preceded by gastrointestinal and grippe-like symptoms. It is self-limited in its course, lasting an average of three to four weeks. Sometimes during this disease, in possibly one-fifth to one-fourth cases, evidence of obstructive jaundice may appear temporarily. During such a phase, urobilinogen may disappear from the urine. However, the presence of associated evidence of severe hepatocellular dysfunction, which ordinarily does not occur in uncomplicated obstructive japndice, will lead to make the correct diagnosis during such a phase.

Extra-Hepatic Obstructive Jaundice

Except for the occasional case of obstructive jaundice in infancy and early childhood, individuals up to the age of thirty are relatively free of this syndrome. In the age group of thirty to

forty, or possibly forty-five, the most common etiologic factors are two: common duct stones, and stricture of the common duct following cholecystectomy. Past the age of forty-five or fifty, new growths of the pancreas, the ampulla of Vater, or of the common or hepatic bile ducts constitute the major cause of this syndrome.

While the etiologic factors in extra-hepatic obstructive jaundice may differ radically in each age group, the clinical features, particularly the laboratory findings, are common to all of these types. The tests for liver function (except when hepatocellular damage occurs late in obstructive jaundice) such as the cephalin flocculation and thymol turbidity are normal. The prothrombin time is decreased but responds to parenteral administration of vitamin K. The serum alkaline phosphatase is elevated and the serum cholesterol and esters is normal or moderately elevated. In complete obstruction the stools are acholic and urobilinogen is markedly diminished or absent in the urine.

Before discussing particular anatomic types of obstructive jaundice in the various age groups, it might be mentioned that unrelenting jaundice occurs only in three types: congenital atresia of the bile ducts in infancy; carcinoma of the head of the pancreas or of the extra (or intra) hepatic bile ducts, and complete stricture of the common bile duct. In all other types, which will be discussed later, the jaundice may relent temporarily or even disappear.

Chlorpromazine (thorazine), arsphenamine, and methyl testosterone may also produce a typical clinical picture of "silent obstructive jaundice." Because of its increasing use in recent years, thorazine, in particular, has come into prominence as a cause of painless jaundice. In the latter case, the pathologic alterations occur in the intra-hepatic bile caniculi which becomes obstructed by bile thrombi. This may occur very rapidly, even after the administration of one or two doses of the drug.

The jaundice may last for many weeks and the laboratory findings completely resemble those found in the surgical types of obstructive jaundice. Should such a patient be known to have gallstones, it is easy to see that a decision for or aganst surgical intervention may become difficult. On the one hand, the impaction of a gall stone in the common duct or ampulla of Vater may be unassociated with pain; on the other, surgery in the presence of thorazine intra-hepatic obstructive jaundice is not indicated and may, in fact, aggravate the patient's condition, producing the so-called hepatorenal syndrome.

The writer has had occasion to explore such a patient who developed thorazine induced jaundice (this was not known prior to surgery). The extra-hepatic ducts were somewhat collapsed and opening the common duct yielded just a few drops of brownish liquid. No bile was excreted through the T-tube until the fourth post-operative day. Gradually, the character of the bile became normal in color and amount. These patients usually recover within three to four weeks (without surgery of course).

The various anatomic or surgical types of obstructive jaundice will be presented according to age groups. It is to be noted that only the first type, congenital atresia of the bile ducts, occurs exclusively in a very limited age group. The age range mentioned for the other types are to be considered as being diagramatic rather than pictorial. For example, while carcinoma of the head of the pancreas usually occurs in persons over fifty, this lesion may occur much earlier in life, the writer having recently operated on a man of forty-one with this diagnosis.

Obstructive Jaundice in Infants

There are three primary causes of obstructive jaundice in infants: erythroblastosis fetalis, where there may occur plugging of the bile ducts by pigment debris from excessive destruction of red blood cells; a similar obstruction without the presence of hemolytic destruction of the red corpuscles in which dried muccous or bile plugs the bile ducts, and congenital atresia of the bile ducts.

In all of these three categories, jaundice may appear at birth or shortly after.

The icterus reaches a high intensity until relieved by surgery, where surgery is possible. Obviously, the first type is easily diagnosed because of the presence of erythroblastosis fetalis. The second type may readily be confused with congenital atresia. The treatment in the first two forms is irrigation of the bile ducts with saline, preferably through the gall bladder.

Gross[1] has classified congenital atresia of the extra-hepatic bile ducts into five anatomic types. This classification is based upon his experience with 146 cases, a large series indeed for this rather uncommon clinical entity. These types are as follows:

1. All ducts and gall bladder, except common duct, present.

2. Hepatic duct and gall bladder present and normal. All other ducts atretic.

3. Gall bladder and all ducts atretic.

4. All ducts except gall bladder atretic.

5. Hepatic duct atretic, remaining ducts and gall bladder normal.

Only the first two types are amenable to surgical attack and in only eighteen per cent of the cases in this series (twenty-seven cases) was re-establishment of bile flow into the duodenum feasible.

Moore[2] recently reported an interesting case of neonatal obstructive jaundice which, from the standpoint of classification, may be midway between the two chief types seen in early infancy — plugging of the bile ducts by debris, muccous, or inspissated bile and congenital atresia. The case was that of an infant with erythroblastosis fetalis for which appropriate treatment had been instituted. However, the jaundice failed to clear.

The total bilirubin rose to sixteen milligrams per cent one month after birth and finally to twenty-two milligrams per cent. The child was operated upon at the age of forty-two days. At surgery, the ducts and gall bladder were present and normal. The common duct was opened and found to contain dried material, which was irrigated. However, an obstruction seemed to be present on probing the proximal portion of the common hepatic duct. Moore felt that a diaphragm type of atresia, such as occurs congenitally in the small bowel, was probably present proximally in the hepatic duct and that he had broken this with his probe.

Obstructive Jaundice in the Age Group 25 to 45

The two most common causes in this group, by far, are stones in the common duct and stricture of the common duct from injury to it during gall bladder operations.

Common Duct Stones

In most clinics, the common duct is opened and explored or probed for stones in about thirty per cent of operations for cholelithiasis. The indications for common duct exploration are: 1) a history of jaundice following colic; 2) dilatation of the common duct; 3) presence of small stones in the gall bladder; 4) the palpation of stones in the common duct.

In about forty or fifty per cent of these explorations, stones are found. However, not infrequently, particularly in older patients in this age group, a stone or stones become impacted in the duct or in the ampulla of Vater prior to cholecystectomy. These patients usually present a long history of biliary disease with many attacks of colic. Often there are previous cholecystograms available, establishing the diagnosis of chronic cholelithiasis. The jaundice, unless a stone completely obstructs the common duct or the ampulla of Vater, is usually intermittent and not unrelenting.

Sometimes a syndrome known as Charcot's intermittent fever may occur. The patient suffers intermittent attacks of right upper abdominal pain, fever, chills, and an increasing degree of jaundice. It should be remembered that not all stones in the common duct result in jaundice and that not all patients with gall stones, or both, necessarily have colic (about twenty per cent). Consequently, patients with impacted common duct or ampullary stones may present a clinical picture of painless jaundice.

It has been pointed out that obstructive jaundice due to stones usually occurs in the ages thirty-five to forty-five. In this age group the stones are usually larger than, say, in younger women in the twenties and early thirties. Not only are they larger, but the stones are more often more ragged and irregular in shape because of the many deposits of cholesterol, calcium salts, and other elements in bile that have accumulated over a period of years.

In the writer's opinion (as well as, of course, in others'), the smaller, round, rather soft, primarily cholesterol stones occurring in younger women (the ratio of incidence of gall stones in this age category in men and women is probably four to one) often pass through the ampulla of Vater, particularly during attacks of colic. This is not to be construed as a plea for the non-surgical treatment of cholelithiasis in young adults. A rather interesting case that the writer encountered five years ago will illustrate this phenomenon.

The patient was a woman of twenty-five who, beginning with the fifth month of pregnancy began to experience frequent attacks of gall bladder colic, three to four attacks per week. These were never associated with jaundice, highly colored urine, or acholic stools. She continued to have these attacks until about six weeks after delivery.

When seen, some three months postpartum, her cholecystograms which had been done one month post-partum, revealed her gall bladder filled with dozens of small stones. The attacks of colic had ceased six to seven weeks prior to surgery. At operation, palpation of the gall bladder failed to reveal the presence of stones. The cholecystograms were unequivocally established as those of the patient.

Cholecystectomy was performed and the common bile duct opened and explored. No stones were found in the duct or in the region of the ampulla of Vater. Examination of the gall bladder after its removal revealed one stone of the size and shape as seen in the roentgenogram impacted in the cystic duct above the clamp. Recovery was uneventful and the patient has since been free of biliary disease.

In the face of jaundice, intermittent or unrelenting, in a patient with known cholelithiasis, surgery should be resorted to after preparation with parenteral vitamin K, other vitamins, and the establishment of fluid and electrolyte balance. If the jaundice completely disappears, it is probably best to wait for a short period (ten to twenty days) to allow the resolution of a cholangitis which is usually associated, and to prepare the patient for sugery.

Obstructive Jaundice Due to Traumatic Stricture of the Extrahepatic Bile Ducts

Almost all cases in this category result from injury to the common hepatic or common bile duct during cholecystectomy. Occasionally, such injuries may result after operations involving the duodenum, or liver, or hepatic fixture of the transverse colon. It is difficult to estimate how many such cases occur each year. In the experience of some surgeons who have had a large experience with these lesions (Gray, Lahey) the frequency is increasing.

The more common ways in which injury to the ducts occur during cholecystectomy are: 1) inaccurate attempts at controlling hemorrhage from the cystic artery with the result that the hepatic duct is partially or completely occluded; 2) undue traction on the mobilized gall bladder when tying the cystic duct, resulting in a similar injury to the duct distal to the ligature; 3) injury to the common duct while exploring for stones which may either produce a fistula between it and the duodenum or injure the duct so that fibrosis results; and 4) more rarely the lower end of the duct may be injured due to excessive "inturning" of the duodenum during gastric resection, excision of a posterior duodenal ulcer, or operations on the liver.

It is apparent that a thorough knowledge of the normal anatomic patterns as well as all the variabilities encoun-

tered during cholecystectomy should obviate these injuries.

J. M. Greene and E. I. Greene,[3] in an anatomic exposition recently at the Illinois Medical Society, presented a review of 200 cases, in which they pointed out in only thirty-eight per cent of their cases was the relationship of the cystic, hepatic, common ducts, cystic and right hepatic arteries "normal."

Not only a knowledge of the "normal" and more common variations essential for safe surgery on the gall bladder, but also careful dissection of the ducts and their anastomoses (cystic duct to gall bladder and to common bile duct), as well as the cystic artery and its relation to the bile duct and gall bladder.

No ligatures or clamps should be placed on the cystic duct or artery before these structures and their relations have been completely visualized by careful dissection. Dissection and division of these structures prior to mobilization of the gall bladder itself is a much more anatomic and safe approach than its dissection and removal from "above downwards." Also careful dissection, visualization, and division (after ligature) of the cystic artery prior to the same procedure on the cystic duct, will also contribute to the safety of the operation.

Usually, the artery is shortened and more taut than the duct. Excessive traction on the duct may injure the artery. Occasionally, when the artery is directly behind the duct and not easily visualized, it is wiser to ligate the duct first after its careful dissection from the vessel. In patients who have had cholecystitis prior to surgery, the right hepatic artery may be adherent to the neck or even the body of the gall bladder.

Failure to recognize this situation may result in injury to this vessel, with its serious consequences. It should be stated that most of the injuries to the ducts during cholecystectomy are inflicted on the common hepatic duct during attempts to control hemorrhage.

Jaundice resulting from injury to the bile ducts may occur a few days after surgery. If the atresia is not complete, jaundice may occur gradually and deepen as the fibrosis progresses. Once the atresia is complete, the jaundice becomes relentless. Some eighty to ninety-five per cent of benign strictures of the bile ducts result from cholecystectomy. Most patients are women (three to one) as gall bladder disease is more common in this sex. The average age is forty to forty-five years.

A rather rare form of benign stricture is chronic obliterative cholangitis, resulting from a slowly progressing inflammatory process which destroys the intima of the ducts and followed by cicatrization. This condition is usually associated with the presence of gall stones. While the process usually affects the whole duct and even the intrahepatic ducts, it is occasionally segmental, thus allowing surgical correction.

While it is not within the scope of this paper to describe surgical procedures in detail, some general remarks illustrating basic priciples may aid in the clarification of this subject.

Those surgeons who have had an extensive experience with the repair of these injuries, agree that whenever possible an attempt should be made at primary anastomosis of the duct, rather than anastomosis of, say, the hepatic duct to bowel. When the latter procedure becomes mandatory because of the unavailability of a sufficient length of distal duct (common bile duct), anastomosis of the hepatic duct and jejunum (with jejuno-jejunostomy below the anastomosis) rather than with the duodenum should be performed. Regurgitation and possible stenosis of the anastomosis is less likely when the former procedure is done.

Lahey[4], reporting 314 cases at this clinic, describes the anatomic varieties of these injuries and the methods of repair employed. These are the methods of repair generally employed. Dragstedt and Woodward[5] suggest a method of direct anastomosis of the duct by mobilization of the portion of the common duct within the pancreas. They feel that such mobilization will make it possible to perform a direct anastomosis rather than

the less preferred choledocho-jejunostomy or duodenostomy.

The all too true adage that an ounce of prevention is worth more than a pound of cure aptly applies to traumatic stricture of the bile duct. A thorough knowledge of the anatomy and its variations, in addition to meticulous care at surgery, would reduce the incidence of this unfortunate sequelae to cholecystectomy to a minimum.

Obstructive Jaundice Resulting from New Growths

New growths that cause obstructive jaundice are situated in three locations: the head of the pancreas, the ampulla of Vater, and the bile ducts. These lesions are almost invariable malignant. Occasionally, chronic pancreatitis, involving the head of this organ (the periampullary portion), or very rarely benign tumors of the extrahepatic bile ducts may be a cause. In the ducts, these lesions usually are adenomas or papillomas and are situated in or near the ampulla of Vater.

Carcinoma of these three anatomic sites cause about as many cases of obstructive jaundice as common duct stones and benign stricture of the bile ducts do together. Carcinoma at these sites occurs in older age groups; those affecting the pancreas and ampulla of Vater in people of fifty and over, and those affecting the bile ducts in an even older age group. Carcinoma of the pancreas affects men predominantly, while cancer of the ampulla of Vater and bile ducts affects both sexes about equally until the age of sixty-five, after which there is a slight predominance in males.

Of the three lesions, cancer of the pancreas is by far the more common, in a ratio of about three or four to one. Two of these lesions — cancer of the pancreas and cancer of the bile ducts — produce unrelenting and severe jaundice once the duct is completely obstructed. In cancer of the ampulla of Vater, ulceration, or possibly attenuation of associated edema, sometimes results in variations in the degree of jaundice.

Carcinoma of the head of the pancreas characteristically produces "painless jaundice," as contrasted with stones in the duct of ampulla of Vater; and also with cancer of the ducts themselves and the ampulla of Vater. In about eighty per cent of cases of cancer of the head of the pancreas, the gall bladder is dilated and can be palpated (Courvoisier's Law).

The outlook for cure in these three lesions is very poor. It is best in cancer of the ampulla of Vater. The reasons for this poor prognosis become apparent on study of the clinical behavior, the anatomic locations, and the low degree of operability of these lesions.

Today it is fairly generally agreed that the Whipple operation (which consists of a radial resection of the head of the pancreas, the proximal duodenum and antrum, the distal portion of the common duct followed by anastomosis of the common duct to the jejunum, anastomosis of the pancreas and its main duct to the jejunum, splenectomy, and a gastro-jejunostomy) should be attempted only in cases where the cancer in the head of the pancreas is small. Experience has shown that the high operative mortality (eighteen to thirty per cent) and the low survival rate even after successful resection, make the simpler side-tracking operation (cholecysto-jejunostomy by the Roux-Y method or cholecysto-jejunostomy with jejuno-jejunostomy below the anastomosis) the preferable procedure.

It is also true that a definite diagnosis of carcinoma of the pancreas by biopsy, either direct or by means of the Vim-Silverman needle, is not often obtainable because of failure to biopsy the carcinoma. Almost every surgeon, who has had experience with this lesion, will tell of occasional patients who have survived more than five years after a side-tracking operation. In these cases it is reasonable to assume that the diagnosis of carcinoma was erroneous if surgical biopsy failed to reveal definite malignant changes.

In contrast, carcinoma of ampulla of Vater offers a better chance for survival. The average length of survival (two or three months) is twice that for the pancreas. Also, this lesion more often lends

itself to a Whipple operation since extensive metastasis, adherence to the portal vein, large size of the tumor, are less frequent with this lesion at the time of surgery.

Even more hopeless with respect to surgical attack than carcinoma of the head of the pancreas is cancer of the extra-hepatic bile ducts. The primary reason lies in the location of these tumors. Of ninety cases from the Mayo Clinic, reported by Niehling[6], the locations were as follows: twenty-nine in the common bile duct, thirty-one at the junction of the common hepatic and cystic ducts, twenty-three in the hepatic ducts, four diffusely situated in the ductal system, and three in the cystic duct.

When it is considered that those tumors in the hepatic ducts offer no chance for resection or a side-tracking operation and that most of those occurring at the junction of the three ducts offer only a little more opportunity for resection or palliation, this lesion becomes quite hopeless. Even with lesions in the common duct, metatases to the hilus of the liver often make palliation or resection very difficult. Some hope for relief in this lesion may lie in experimental work with grafts to replace the bridge defects in the common bile duct[7].

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MEDICINE AND LAW IN THE BIBLE*

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In a recent symposium on "The Relation of Religion to the Practice of Medicine and the Training of Doctors," the Associate Executive Dean for Medical Education and Professor of The History of Medicine at the State University of New York, Dr. J. A. Curran, introduced his remarks with this observation:

"While in the modern medical curriculum there are no assigned hours devoted to the part religious concepts and ideals that have played in bringing medicine to its present high standards of service to suffering humanity, those values are taught by precept and example, often unconsciously. Furthermore, there are concrete evidences that faculty and students alike are showing growing interest in religious fundamentals and relationships thereof, to their professional lives. Significantly, this mounting awareness has been paralleled by an increasing appreciation of the value of historical, cultural and philosophical contributions to their scholarly maturity, as wise and understanding physicians. Obviously, all these developments are closely related both in their backgrounds and their relevance to the present world in which the doctor of medicine must plan his difficult roles of scientist, counsellor, friend and guardian of the people's health."

What Dr. Curran has to say about the heightening interest of teachers and practitioners of medicine in the teachings and practices of religion and their relationships to their profession, applies equally to the rules and decrees of law. Medicine cannot operate in a vacuum.

It deals with human beings, not only with their bodies and minds, but also their hearts and souls. It contacts and concerns itself with them not only as individuals, but as groups, social and political as well as racial and religious. It must consider the complete man, everything that he is and all that touches his life, and not just what the eye can see and the ear hear.

Today we understand much more clearly than when it was first utttered, the old truism: *Man ist wass man isst,* one is what one eats. That means that the whole human being is what he takes in physically, but may I also say mentally, emotionally, and spiritually. And in addition, he is also what is taken from him physically, mentally, emotionally and spiritually.

There is a story about Goethe—it may be fiction not fact—that when he was visiting Rome on his Italian journey, he saw some poorly dressed blind beggars in front of St. Peter's holding up to the passers-by, crudely scrawled appeals. His curiosity was aroused when he discovered that while most of them were ignored, there was one into whose cup a coin was dropped by practically every worshipper and visitor who came that way. In fact, some of them who had failed to make a donation, turned back, apparently conscious-stricken and they, too, contributed to this specially favored beggar.

Unable to restrain himself, Goethe joined the procession and passed by each one of the blind men, carefully scrutinizing them and reading their signs. Everyone of the signs, except that of the very successful beggar, read: "Help the Blind." His read: "It is April and I am blind."

Medicine and Law often fail to make the proper analyses of cases and achieve good results, not only because they are blind or ignorant of the facts, but also because they forget about it's being "April." They fail to remember that there are many factors and features connected with their cases that appear to be unimportant and insignificant, but

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which are really substantial and must be examined and entered into the total picture before any adequate evaluation can be made.

That is also true of religion, generally regarded as their mother, that gave them birth. When the field of religion is provincial and not universal in its interest; when it teaches life only partially, not totally; when it is merely a narrow by-way for the chosen few instead of a broad highway for the countless many, it too fails to make proper analyses and achieve good results.

May I at the outset make quite clear, as a religionist, being a representative of the extreme liberal wing in Reform Judaism, that my approach to the Bible is as objectively scientific and unhesitatingly critical as is that of the clinician in the examination of a specimen in a research laboratory. For example, the discovery of the Dead Sea Scrolls holds no terrors for me. I do not tremblingly fear any possible new light they may shed on the origin, the nature, the purpose, the value of our sacred scriptures. On the contrary, I eagerly welcome whatever illumination they may throw into the many dark areas and corners which are still shadowy and vague in their inspiration as well as information.

It is quite possible that these Scrolls may clear up much that is still confused and controversial in the world of religion; that blinds us to the basic visions and needs in human relationships and prejudices us against and divides us from millions of our brothers. Perhaps it will help us to remember in our blindness that it is "April" and that life's most wonderful gift still remains the privilege of just being alive and being able to see and experience the wonders of this earth.

To me, the Bible is a human document inspired by God, but inscribed by man; not delivered at one moment at about 1300 B.C. to one man, Moses, at one place, Mount Sinai, in the wilderness, but developed over a period of 1000 years, from approximately 1150 B.C. to 150 B.C., by numbers of prophets and priests, scribes and sages, in different parts of Palestine, but probably also Babylonia, Assyria, Persia, Syria, Greece, and possibly Egypt. The Bible is the historical statistical record of a people's search for God and its efforts to translate His word and His way into their lives and loves and labors.

Everyone of the Books speaks the language of the time and locale of its creation, the medical and legal, as well as the moral and ethical language. Even as it is possible to chart in its pages the gradual progressive changes in the concept of God, as it grows from that of a primitive murderous deity of wrath and vengeance to the more advanced civilized Father of mercy and love, so one can trace similar evidences of advancing change and growth in all areas of human beliefs and behavior, aspiration and activity.

In the realm of scientific knowledge and accuracy, the Bible is woefully inadequate when compared with the books of our time. But in the field of spiritual vision and value, it stands at the very summit of human understanding and wisdom, still unmatched and unsurpassed.

A number of excellent articles and books have already been written to acquaint us with the presence of many passages in the Bible testifying to the ancient Hebrew people's awareness of the necessity of medical treatment and legislative enactment. There are quite a number of references to various types of diseases, methods of healing, and the use of physicians in the modern sense.

Of course, the Bible is full of laws issued by the Divinity and to be enforced by the community in His name. In this paper, since it is possible to find other valuable sources for such material, we shall not concern ourselves with the citation of Biblical book, chapter and verse, as proof of the remarkable contributions made by the ancient Hebrew in these very vital fields of human creative achievement.

The definite need for the knowledge and application of both medicine and

law is clearly recognized in the Bible, more so in the case of law than in medicine. But the knowledge is quite limited and the application primitive. Progressive growth in the theories and techniques of their practioners is not so readily discernible, less so in the case of law than in medicine.

The Bible praises God as the source of all health and happiness as well as life and love. Ultimately, it is the Divine Power that heals and helps man conquer disease and even death. They who minister to human ills, those of the body and mind as well as the spirit, are God's messengers. In the primitive period, they were priests whose function was not so much that of healing the disease-stricken, but that of supervising their care and protecting the community from contagion. There are instances of prophets effecting miraculous cures and bringing the dead to life.

In the Book of Kings we have the case of a man of God restoring the dried-up immobile hand of King Jeroboam through prayer, and of the Prophet Isaiah curing an inflamation of King Hezekiah that had made him sick unto death, by applying a cake of figs to a boil.

The Bible, however, indicates that physicians, separate and apart from the priests and prophets, were practicing their profession in those earliest days. The Book of Genesis speaks of Joseph as sending physicians to embalm his father. The Book of Chronicles is critical of King Asa who had some serious foot disease for employing physicians instead of entreating the Lord in his search for a cure. Jeremiah reveals the established place of medicine and its practice when he asks: "Is there no balm in Gilead; is there no physician there?" The Book of Ecclesiaticus, written by Jesus Ben Sirach, which for some inexplicable reason was excluded from the Canon of the Bible and retained in the Aprocrypha, exhorts: "Honor a physician with the honor due unto him for the uses of which ye may have of him, for the Lord hath created him . . . The Lord has created medicines out of the earth; and he that is wise will abhor them . And He has given unto men skill that He might be honored in His marvelous works . . . Ye son, in thy sickness, be not negligent . . . give place to the physician . . . let him not go from thee, for thou hast need of him."

There is evidence in the Bible, though most of it is oblique and inferential that its writers possessed some medical knowledge. They had some understanding of anatomy. It speaks of the veins and gall and vessels filled with fluid, and marrow of the bones, the abdominal muscles, the generative organs. They knew something about embryology and surgery. Although they mention only circumcision and castration, they probably performed other operations of ex ternal nature, and possibly some that were internal. Wounds of almost every type; discharges and abscesses; gangrene and leprosy are not only noted, but treatment is prescribed.

An objectively critical and intelligently careful study of the Bible does not bear out the exaggerated partisan claims that have been generally made in behalf of the Bible as a remarkable textbook of medical and legal knowledge and achievement.

It is well established that centuries before the first Biblical document saw the light of day, both medicine and law were already established as very vital parts of the great civilizations of Egypt and Babylonia. Authentic sources of information reveal that Egypt was probably the medical center of the Middle East during Hebrew bondage.

In his paper published by the Pennsylvania Medical Journal (April, 1952), "Biblical and Talmudic Medicine," Dr. Benjamin Lee Gordon points out that Egyptian medical papyri of that time indicate that "both surgery and medicine made phenomenal strides . . . Amputations of the legs and arms were performed, the bladder was opend for stones; cupping and blood letting were prevalent practices; and coughing for cataract was performed. Ancient Egyptian mummies show that decayed teeth were filled and

artificial teeth of gold were employed to replace missing teeth. This being the case, it is difficult to conceive that during the centuries of bondage, the Hebrews did not learn of the Egyptian medical tenents . . . The fact that early Jewish medicine was based on principles of still earlier medical knowledge does not in any way detract from its usefulness and glory."

Of course, the probability that the ancient Hebrews gathered much of their information and inspiration for medicine, and also law, out of their unhappy association with the Egyptians, does not in any way detract from the genius and value of their own contributions in these fields, any more than the probability that Moses gained his information and inspiration for his monotheistic conception of the universe out of his association with that ill-starred Egyptian, Prince Amenhoteph IV (Ikhnaton). But the truth is that the Bible does not even match the Egyptian payri, much less surpass them in either wealth or growth of medical knowledge of application. The truth is that the Bible does not contain enough convincing evidence to prove that its writers knew very much about medicine and its practice as we know them today.

By way of apology, Dr. Gordon explains "the absences in the Old Testament of diseases and drugs mentioned in the Egyptian papyri may to some extent be due to the strict hygenic restrictions of the Old Testament. The distinction of Hebrew medicine of that period does not lie in the diagnosis and therapeutics of disease but in the realm of social hygiene and preventive medicine. The anticipation of this modern concept was bound to promote the welfare of the ancient Israelites and contribute toward the preservation of the future nation. Prevention of epidemics, supression of prostitution and veneral disease, frequent ablution, care of the skin, regulation of sexual life, dietary laws, and observance of the Sabbath, have tended to cut down the prevalence of disease among the Israelites."

It is difficult to understand why strict hygenic regulations could discountenance the mentioning of the diseases and drugs recorded in the Egyptian payri. On the contrary, if their use was regarded as dangerous or sinful, a clear prohibition would have been an added safeguard. The Bible is particularly explicit in its "thou shalt nots." It is almost pathologic in its admonitions against "whoring" after other gods, which usually means the preachments and practices of other peoples. Also, much greater care should be exercised in the ascription of a special distinction to the writers of the Bible for original creative contributions in the field of social hygiene and prevtive medicine. So much of what is considered as prophetic and purposeful in these areas was only coincidental or accidental.

As an example of the extreme lengths to which one can go in the effort to prove the presence of real medical knowledge in the sacred scriptures, we can turn to almost any page in Dr. C. Raimer Smith's volume, "The Physician Examines the Bible." "The Hebrews," he writes, "unlike their neighbors the Egyptians and Babylonians, left no medical literature *per se* but the Bible contains many references to medical subjects." Then he proceeds to give specific examples. We shall select at random three such examples at the very beginning of his book, which are typical of all the ramainder.

"A good description of an attack of angina pectoris," he says, "occurs in Ps. 55:4-5 (also Proverbs 14:13, Jeremiah 48: 41; 8:18; Lamentations 3:65), 'My heart is sore, pained within me and the terrors of death have fallen upon me. Fearfulness and trembling have come upon me and horror hath overwhelmed me'." Angina is a sudden attack of severe pain over the heart, frequently accompanied by a feeling of impelling death—sometimes anginal pain is referred to the abdomen."

He quotes Ezekial 7:7: "All hands shall be feeble and all knees shall run with water," and comments, "water on the knee occurs in cases of injury and inflamation of the knee joints, as arthritis

and bursitis." Taking Psalm 129:2-3: "Many a time have they afflicted me from my youth yet they have not prevailed against me. The plowers plowed upon my back; they made long their furrows." He asserts he cannot imagine these verses being inspired except by a backache as certain types of backaches can really torture a person and he can easily imagine many plows making deep their furrows."

Any student of the Bible might easily point out the general tendency of its writers to express their thoughts in poetic form, using similes and metaphors, words and phrases, figuratively, not literally. There are numerous verses which depict a sense of emotional dis tress and spiritual despair as a pain in the heart and the threat of death. Some phenomenon of water is often used to describe human feeling or conduct. Farm implements, like the threshing sledge and the pruning hook, and their uses, are often employed to make graphic, human experiences.

Perhaps even more extreme are the efforts of Dr. Charles I. Brim, in his "Medicine and the Bible." One example will suffice: "Except for a few specific instances," he writes, "the Pentateuch does not give us very much information regarding the surgery of the Biblical era. Surgical operations, however, were performed and who knows but that anasthesia may have been employed. An accurate description of the first surgical operation performed after the manner of modern operative work is sketched in simple and direct language when the Lord performed the famous rib-resection operation upon the first man. The five steps of the operation are recorded as follows:

(1) "And the Lord God threw a sleep on Adam." (beginning anaesthesia)

(2) "And he slept . . ." (deep anesthesia)

(3) "And then God took out one of his ribs." (the operation)

(4) "And then he closed the wound." (suturing)

(5) "With flesh." (skin graft) "to replace the ugly scar which had resulted."

It is not only the Devil who can quote scriptures to suit his ends.

Some of the best known and generally accepted proofs offered to establish the existence of Biblical knowledge and application in the field of social hygiene and preventive medicine are the laws of circumcision, cleanliness, and diet. It has become a matter of common and wide-spread belief that health reasons were behind the commandments for circumcision of every male child; behind the regulations dealing with women in their menstrual and after-birth periods; behind the proscription against the eating of certain foods or eating them in certain mixtures, or eating them at certain times. But the probability, based upon the best scientific Biblical study, is that most of the commandments ascribed to concern for healthiness were really connected with holiness. Moses was not a sanitary officer but a sanctity officer. And his brother Aaron, when supervising diseases, especially those of the outer skin and genital tissues, and policing their recoveries, was not a physician, but a priest. They were concerned more with the commandments of God than with the cures of man.

The prevalent popular explanation of the origin of the rite of circumcision, a rationalization and justification, is that it was wisely designed as a health measure. The truth is, as anthropoligical studies reveal, that in its primitive form, circumcision was performed with a view to marriage, either for the facilitation of cohabitation or as a consecration of the generative function. In the Bible it is a mark of kinship to Abraham, the first Jew, relationship to the people Israel and faithfulness to God. Its health value, if at all considered, was only incidental, not fundamental in the minds of the ancient Hebrews.

The old saying that "cleanliness is next to Godliness" applies with special pertinence to the Biblical regulations dealing with the touching of unclean

persons or places, or the possessing of unclean things or thoughts. The probability is that healthiness was a later by-product rather than an original basic purpose. That which was unclean and ugly was an abomination in the eyes of the Lord. A priest was forbidden to touch a corpse, except that of a close relative, because it was unclean in itself, even if it were that of a healthy and saintly being.

The usual explanation, and again only an after-thought of rationalization and justification, for the maintenance of the Biblical and Rabbinic dietary laws is that they keep the person and people healthy. If so, and statistics taken among the very few who still scrupulously observe the laws, do not conclusively prove this view to be correct, again, it is only incidental, and not fundamental. In the Bible, we find that the ancient Hebrew people were forbidden to eat certain animals, birds and fish declared unclean, or certain parts of animals or the torn flesh of certain animals, merely on the ground that they were an abomination in the eyes of the Lord and Israel was bound to be a holy people unto God. Other reasons have been given, such as that the flesh of carnivorous beasts and birds fills the person with a spirit of cruelty.

It is significant to find that practically all the animals forbidden in the Bible are the same as those prohibited to the priests or saints in the ancient Hindu, Babylonian, and Egyptian laws. And it is highly significant that among these peoples, as well as among primitive peoples, certain animals are forbidden as food for a special holiness they are supposed to possess. That is why the theory has been advanced and supported by those of a scientific temper that since almost every primitive tribe has held specific animals as taboo, the tabooed animals were originally adored, not despised, worshipped as the totems of the clan.

Whether the Bible's primary interest was in holiness or healthiness will always remain a moot question. Did the urgent need for medical treatment and social hygiene influence the priests to set up an elaborate system of the laws of holiness, or did their conception of holiness possibly include healthiness of the body as well as the spirit and inspire them to establish regulations under Divine decree which experience and observation had taught them would aid in the preservation of a healthy and happy and therefore holy community?

In the Bible, all regulations, whether they be medical or legal, or social or economic, or political, are commandments of God. Among the ancient Hebrews, and it might also be said of the Jewish people today, there are no clear-cut distinctions between the obligation for an individual to respect his neighbor's person and property and the duty to worship God with proper devotion and sacrifice. All the commandments carried the same weight of validity and authority, because they all had Divine sanction, stamped by the seal of God.

The word *Torah*, which is usually applied only to the scroll containing the first five Eooks of the Bible in the original unpointed Hebrew text, still read in a yearly circle in all the synagogues in the world, originally meant a teaching rather than a Commandment. For a teaching becomes a Commandment when its source is said to be Divine. Then a compilations of laws fixed in a code-book becomes a Bible when it is handed down as the Sacred Word of God, to be disobeyed at one's peril.

In the Bible, the evolution of law can be traced clearly in the various codes which were created in different parts and places, by different groups of persons and peoples in Palestine. There is the J Code of the Northern Kingdom of Israel, and the E Code of the Southern Kingdom of Judea — creations of the ninth century, B.C. There is the D Code of the Book of Deuteronomy, promulgated probably in the seventh century, B.C.; and the P Code of the Book of Leviticus, fashioned probably in the fifth century, B.C.

Scientific Biblical study indicates that

the well-known and oft-quoted Ten Commandments were not given in their exact form to the people of Israel by Moses at Sinai in the wilderness, but are later and more advanced refinements of earlier more primitive codes, some of which are preserved in the same Book of Exodus where one of the two versions of the Ten Commandments is to be found. The P Code's commandment, "Love thy neighbor as thyself," is a far cry from the command found in the earlier codes: "Thou shalt give life for life, eye for eye, tooth for tooth, hand for hand, foot for foot, burning for burning, wound for wound, stripe for stripe." The ancient Rabbis very quickly interpreted this primitive passage to mean "Compensation for a life, for an eye, *etc.*"

There can hardly be any question that law in the Bible was very markedly influenced by Egyptian and especially Babylonian legislation. There is a very notable similarity between the commandments in the codes, including the Ten Commandments and the commandments in the famous Babylonian Code of Hammurabi, written in the 2300 century, B.C. In his, "The Dawn of Conscience," James Breasted goes so far as to assert: "As a young Orientalist, I found that the Egyptians had a standard of morals far superior to that of The Decalogue over a thousand years before the Decalogue was written," though he concedes that the chief contribution of the Hebrew genius to the One-God idea was his moral nature.

But again, Biblical law, like Biblical medicine, grows out of the special needs of the people. It is quite obvious that it was intended for an agricultural not a pastoral people and designed for a community firmly established in a country such as Palestine. For example, we find one law after another like the Sabbatical and Jubilee requirements for rest and restitution of the land promulgated to prevent the accumulation of great estates and to keep holdings within small family groups. Much of the legislation concerned with land property, ownership of slaves, loans and pledges, bailments and torts, was enacted in order to protect property rights. Though the legislation deals with purely mundane and material matters, yet it is all part of the Biblical Code carrying the authority of Divine Commandment.

Among the ancient Hebrews, law — Divine Law — was not only the fountain out of which was drawn its stream of authority, but law—human law—always thrust back into that Divine stream as its source of sanction was the force used for the maintenance of control over the community. Here too, however, we often claim too much, as in the case of medicine, for the original genius and creative contribution of the Biblical code-makers. The greatness of the Ten Commandments and the laws of health, is revealed in their moral grandeur, not in their legal acumen. They are excellent workman-like rules for the keeping of law and order in a primitive society, but most of them are still spiced with ancient superstition and outworn tradition, yet probably far superior to those of other peoples who preceded and surrounded them. It required much explanation and expansion on the part of the teachers in Rabbinical literature to lift the law of the Bible to the lofty heights of understanding and wisdom in their application to the affairs of man and the visions of God.

The Bible tells us that when Moses brought the first set of tablets containing the Ten Commandments down from Sinai, he smashed them to smithereens when he found the people of Israel worshipping a golden calf. We are led to believe that the Lord would not let him present the second set of the Commandments until the people had foresworn their idolatry, the adoration of the work of their own hands, and revealed their readiness to follow the true word and way of God.

There is grave danger in Bibliolotry—the blind fanatic worship of the Bible as a sacred sure guide for modern man in all areas of human belief and behavior, activity and inspiration. We must remember that the Bible is a human document, written by towering figures of

thought, inspired by the Divine spark, but chained to the human spirit. A spirit that can rise above and beyond its earth environment in moral and ethical idealism, saintly sacrifice and service, must remain forever shackled and limited to the knowledge and understanding of its period of time and place of habitation, in all mundane material desires, drives and dreams. There is danger in adoring the Bible too much and in too many things, even as there is grave danger in not adoring it enough and even not enough of its Commandments.

The Bible must not be made the golden calf of medicine and law. It must not be considered as sacro-sanct—certainly not in the fields of medicine and law. We must beware of ascribing to its writers knowledge and understanding in areas which were not their main concern. We need not read into its pages a greater knowledge and understanding than they had in order to establish the extraordinary stature of its prophets and priests. The spiritual summit on which they stand towers so high that it dwarfs whatever possible peak of scientific achievement they attained.

Let us be content to marvel rather at their extraordinary realization, remarkable for a people living in that ancient primitive world, the capacity to perceive the intimate relationship between religion and medicine, religion and law, and the connection between all three—though in a rather intuitive crude fashion—the nature and importance of which relationships our generation is just beginning to grasp.

Let us be grateful for their vision of not only God as one, the Creator of the entire universe and the Father of all mankind; but of life as one, each part inexorably related to the other part, and all parts indivisibly connected with every other part, and all parts related to the whole; and of man as one, every portion of him—the physical, the mental, the emotional, the spiritual—every portion bound up with every other portion, each affecting the other and reacting to the other, and all making up the whole man.

Let us learn the wisdom of making the Bible, *i.e.*, its moral ideas and ideals, its spiritual values and visions, a part of medicine and law of our time, even as our fathers made medicine and law parts of the Bible of their time.

CLINICOPATHOLOGIC CONFERENCE

DR. L. FELDMAN, Chairman **DR. H. RAPPAPORT, Secretary**

Presented at Mount Sinai Hospital, Chicago, Illinois

Clinical History

First and Final Admission: This 44 year old white male was admitted to Mount Sinai Hospital, September 20, 1954, complaining of itching, anorexia and jaundice of one week's duration. The patient had a cough for several years with moderate expectoration. Prior to admission his urine had become dark in color and the stools remained normal in color and consistancy, with no change in bowel habits. At no time did the patient show hematemesis.

Past History: The patient had diphtheria at the age of eight. He had been a heavy drinker for ten years, consuming about one-half pint of brandy per day. In 1953 he was admitted to Cook County Hospital because of pedal edema which had recurred occasionally at the time of admission to this hospital. While at Cook County Hospital a diagnosis of Cirrhosis was made and Endomeba histolytica was also found in the stool.

Physical Examination: The patient was a 44 year old, well developed, white male who appeared to be ill. His pulse was 94, temperature 100.8, respirations 24, and blood pressure 125/80. The sclera were icteric, the apex of the heart was at the midclavicular line. Apex rate and rhythm were regular and no murumrs heard. A few coarse and moist rales were heard in the right infrascapular region. The abdomen was distended with the presence of ascitic fluid. The liver was enlarged down to the navel, was hard, tender and had a slightly rough surface. There were no venous collaterals on the abdominal wall but a few spider angioma were present at the costo-abdominal line. The spleen was not palpable. A four plus pitting edema of the pretibial area was present. The skin was deeply icteric colored. The testicles were small and soft.

Hospital Course: While in the hospital the patient had a severe, spasmodic, productive cough which on several occasions kept him awake all night. He also complained of recurrent abdominal pain. On September 29th, he became semicomatose. His tongue was swollen and red. Pulse was 100, temperature 100.6. On September 30th, he fell out of bed but apparently was not injured. On September 29th, the stools became loose, foul smelling, and liquid. 2000 cc. of fluid was obtained by paracentesis on September 30th. On October 2nd, he became more alert, although his general condition remained unchanged. Continuing a downhill course, he died on October 4, 1954.

Discussion

Dr. H. Rony:* On admission this patient had an enlarged liver, a few spider angioma, edema of the legs, and ascites. The testicles were small and soft. He also had a marked macrocytic anemia leukocytosis, and an increased reticulocyte count. The serum bilirubin was high, the urine contained bilirubin and urobilinogen, and there was a marked icterus. The percentage of cholesterol esters was low, the alkaline phosphatase was increased, and there was a positive cephalin-cholesterol flocculation test. Although total protein was within normal limits, the serum albumin was low and the A-G ratio was reversed. All of these findings are consistent with an active, proliferating, necrotizing hepatic cirrhosis.

There are some other points, however, which deserve mention.

First, the patient had small and abnormally soft testicles, but normal amounts of chest, pubic, and axillary

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LABORATORY DATA

Hematology:

	RBC	Hb	C.I.	WBC	Myelo.	Meta.	Stabs	Segs	Eos	Bas	Lymph	Mono
9/20	2.78	11.1	1.25	30,750	1	1	4	86	1	1	4	2

Macrocytes-4 plus; 1 nucleated RBC/100 WBC; Rare Howell Jolly Bodies; toxic granulation-1 plus; hyper-segmented polys present.

9/22	2.34	10.4	1.41	31,500	2	1	3	83		1	4	6

Macrocytes-4 plus; 2 nucleated RBC/100 WBC; toxic granulation-2 plus; occ. target cell; basophilic stippling-3 plus; polychromatophilia-3 plus.

M.C.V. 137 cu. mic. (Normal 82-92); M.C.H. 44 (normal 27-31); M.C.H.C. 33 (normal 32-36). Volume index 1.57. Saturation index 0.98.

9/21 Prothrombin Time 19 sec. Control 14 sec. Clotting activity 55%

Corrected Sed. Rate 33. Hematocrit 35. Kahn and Kline negative.

9/22 Reticulocyte count 17.4%. Hematocrit 32.

Urines:

	Color	Sp.Gr.	pH	Prot.	Sug.	Acet.	Casts	RBC	WBC	Bact.
9/21	lt.am.	1.015	5.5	0	0	0			1-3	occ
9/27	dk.am.	1.011	5.5	0	0	0	15-20 (granular)		0-3	few
9/29	rd.br.	1.017	9.0	tr	0	0		occ	8-10	num
10/4	dk.y.	1.010	6.0	0	0	0	3-5 (hyaline)		6-8	num

9/22 24 hour urine. Total volume 1,070. Bilirubin positive. Urobilinogen 2.3 E.U.

Chemistries:

	9/21	9/29	10/4
Total Protein	6.51 gm		
Albumin	3.2 gm		
Globulin	3.31 gm		
A/G Ratio	0.97		
Total Bilirubin	24.4 mg	20.4 mg	
Direct Bilirubin	15.2 mg	11.3 mg	
Total Cholesterol	208 mg		
Cholesterol Esters	14%		
Thymol Turbidity	4.2		
Ceph. Chol. Floc..	3 plus		
Alkaline Phosphatase	11.2 B.U.		
Urea Nitrogen	13.3 mg		62.0 mg
Serum Glucose	121 mg		
B.S.P. Retention		56%	
Serum Creatinine			1.96
Serum Chloride			98.4 meq
Serum Potassium			1.9 meq

EKG one hour before death:

Rate 100

Depression ST_2 Right axis shift. T_1 isoelectric T_2 diphasic

T negative in V_2, V_4, V_6, AVF

hair. The patient asserted that there was no loss of hair at any time during his entire illness. As you know, it is believed that in hepatic cirrhosis the ability of the liver to inactivate the relatively small amount of female sex hormone produced in the male is impaired, with the result that estrogen accumulates in the system and is responsible for the loss of body hair and the atrophy of the testicles. In this case, the testicles were definitely small, perhaps one-third or less of the normal size, but the body hair was not affected.

This is remarkable in view of the fact than an amount of estrogen that would cause atrophy of the testicles certainly would have caused as well the loss of body hair. It has been suggested that the atrophy of the testicle in hepatic cirrhosis is not an estrogenic effect, but a nutritional one. The case under discussion might be regarded as supporting this point of view.

Another point of interest is the marked anemia of the patient. Anemia of the macrocytic type is not unusual in hepatic cirrhosis although severe anemia usually does not occur until the later stages. We know, however, that this patient has a severe anemia for a year before he died.

The leukocytosis, too, puzzled me for some time. Moderate leukocytosis is not rare in hepatic cirrhosis, but this high degree of leukocytosis is very unusual. The fact that is was associated with an increase of polymorphonuclear leukocytes suggested some form of infection complicating the hepatic cirrhosis.

We could not demonstrate a pneumonia. The patient did have a few dry and moist rales in the middle lobe of the right lung but no definite signs of pneumonia were found on repeated examinations.

At Cook County Hospital, where the patient was treated a year before his death, Endomeba histolytica was found on stool examination, and I was wondering whether or not the patient had an amebic asbscess as a complication. However, the liver was diffusely enlarged and there was no limited mass palpable. Thus, I did not entertain the idea of an amebic abscess very seriously. Probably, but rarely, such marked leukocytosis can occur in hepatic cirrhosis without any particular complicating infection.

The patient died in a coma which had all the features of a hepatic coma. Still the question exists whether there was an admixture of uremic coma present as part of what is called the hepatorenal syndrome. However, the urine was not remarkable at any time. Five days before death the specific gravity was 1.017. There was no albumin in the urine and the sediment was not remarkable at any time. There was no anuria, and while there was a pre-terminal increase in the blood urea nitrogen and creatinine, I think that one is not justified to assume that the uremic element is important in the patient's death.

The question that was foremost in my mind in observing the case was whether the patient had a hepatoma as a complicating feature. It is known that hepatoma is not infrequently preceded by hepatic cirrhosis. The somewhat rapid downhill course is remarkable if one considered this to be a case of hepatic cirrhosis and nothing else. The patient was ill altogether for about three weeks, two weeks in the hospital, and one week before admission.

The liver was very large, which is uncommon in late hepatic cirrhosis; it was down to the umbilical line, and very hard. The surface was diffusely rough but there was no discrete tumors palpable. Still, as an outside possibility, I considered hepatoma, and stated in the death certificate that death was due to hepatic coma as the result of hepatic cirrhosis and possibly hepatoma.

Dr. A. J. Levine:* First, I would like to speak about some of the findings mentioned in the physical examination. It is said that the spleen is not palpable. The correct thing to say was that the spleen was not palpated. If the spleen

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was not palpated it would perhaps help to rule out certain possibilities. Among the possibilities that should be mentioned is hemolytic anemia.

An acquired hemolytic anemia can give you a picture very similar to this, such as an enlarged liver, a blood picture which could explain the leukocytosis, and, in the long run, finally the liver itself. You would expect, however, to find a large spleen. If the spleen is definitely not enlarged, it would tend to rule this possibility out.

Target cells, the type of cells mentioned here, go along with the low hematocrit and the macrocytic anemia which give these large thin flat cells which are found frequently in liver cirrohis. One does not have to look far afield to explain the type of anemia, the the target cells, and the reticulocytosis, although the latter is higher in this case than what is generally mentioned as being present in cirrhosis of the liver. All of these could go along with just a cirrhosis, or with a cirrhosis with a florid or a necrotizing hepatitis at the end. Lichtman mentions a reticulocytosis occurring in approximately thirteen per cent of cases with cirrhosis.

The leukocytosis and the increased sedimentation rate are a little harder to explain. In the early phase of infectious hepatitis, when the serum bilirubin is high, the sedimentation rate is low. If the sedimentation rate is high at this point, you almost certainly do not have an infectious hepatitis. That appears later on, somewhere in the second or third week, when the serum bilirubin returns to normal levels. These two laboratory values, the leukocytosis and the increased sedimentation rate, do not fit too well, even if we theorize that a necrotizing hepatitis is also present, unless we find something else to explain them.

The patient had a diarrhea that may have been due to a phlegmonous entrocolitis, which can occur in a terminal stage of hepatitis, or possibly a carcinoma, either metastatic or primary, within the liver itself. Amebic abscess, of course, is a possibility, although I think that the liver function tests show that a more widespread hepato-cellular damage, such as is associated with cirrhosis, was present.

As I am being called upon to express an opinion, I think I will go along with Dr. Rony that this is a Laennec cirrhosis with a florid end stage of a necrotizing hepatitis, with the unusual blood picture that can be occasionally found in a cirrhosis, and a complicating infection, possibly an enterocolitis or a pulmonary infection, to explain the leukocytosis and the increased sedimentation rate.

Dr. H. Isaacs:* The electrocardiogram throws no light whatsoever on the clinical picture. The electrocardiogram is compatible with chronic coronary insufficiency, although some of the T wave changes may be due to anoxia on an anemic basis. There are no previous

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Figure 1

Liver. Portal Cirrhosis. A typical parenchymal regeneration separated by branching connective tissue bands. Note the extensive necrosis of the parenchymal cells. H. E. 130X.

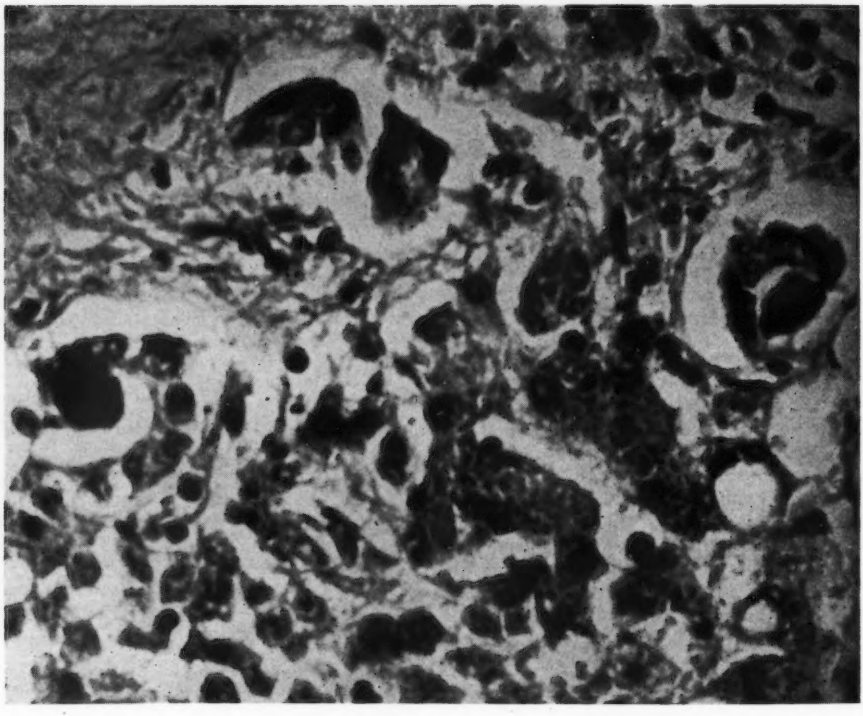

Figure 2

Same as Figure 1. High magnification of the necrotic parenchymal cells. H. E. 720X.

electrocardiograms available for comparison.

There are some other facts present in the history which I feel should be discussed. The history presents a few points that can speak for a Laennec Cirrhosis. I would like to point out that these cirrhotics, who have had findings for many years, usually show little or no anemia unless there is massive hemorrhage present also, as from esophagal varices.

When a patient has a glossitis, an anemia, with a reticulocytosis, one should always think of pernicious anemia. The differential count and examination of the bone marrow would solve this problem quite easily, although the therapeutic response with liver therapy would aid considerably. I might have done a marrow puncture in this case to rule out this possibility. Gastric analysis may not be too helpful in this particular case because an achylia gastrica which is associated with pernicious anemia can also occur in an alcoholic gastritis.

In a given case of edema, ascites, and hepatosplenomeglay, the edema can be due to hypoproteinemia. I have seen a number of patients with pernicious anemia who are dyspneic because of their anemia, have a functional systolic murmur at the apex, and anasarca, being treated for heart failure until somebody suspects the presence of a blood dyscrasia.

Lastly, this patient had liquid, foul smelling stools. Whenever this occurs, one should always suspect pancreatic involvement.

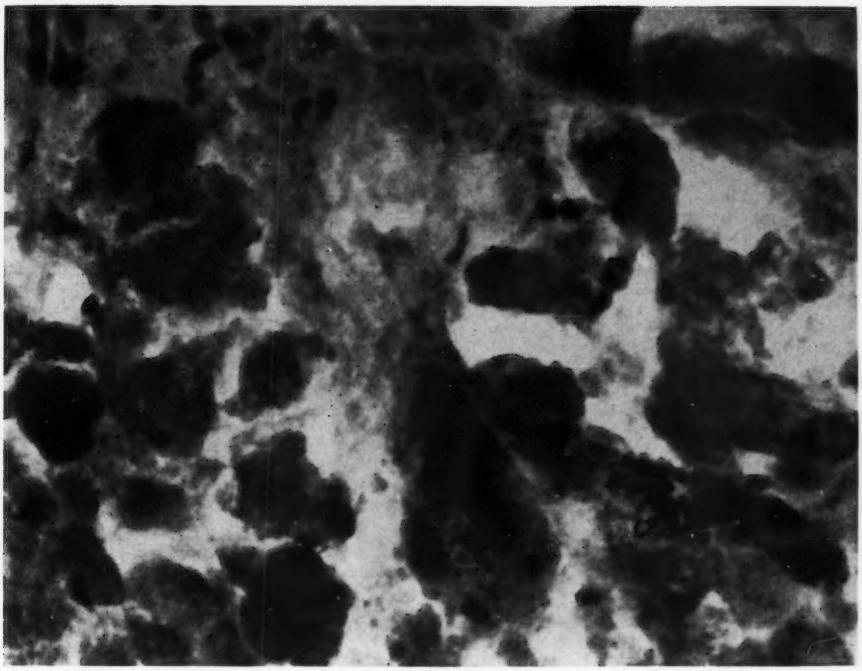

Figure 3

Liver. Portal Cirrhosis. Bile canaliculi containing "bile thrombi." H. E. 680X.

Dr. B. Pearlman:* This patient presents a clinical course which we commonly see in our wards at Cook County Hospital. Many patients with chronic alcoholic cirrhosis go along quite well with no overt evidence of hepatic failure. After discharge, they imbibe large amounts of alcohol and return very ill in a state of acute hepatic failure, *i.e.*, fever, jaundice, semi-stupor, vomiting, and a diarrhea which often has a positive benzidene reaction. Dr. Popper has discussed this problem over and over again. I believe that he used to call this an "acute toxic hepatitis," but I think he now refers to this situation as just an acute hepatitis superimposed upon a chronic cirrhosis. The prognosis is usually grave and many of these patients die within a short period of time of an acute hepatic necrosis.

While the diarrhea may be due to various causes, many of these patients come in with a severe diarrhea. Autopsy usually reveals an acute hemorrhagic colitis or a pseudomembranous colitis. Another cause of death, aside from acute hepatic insufficiency and coma in this patient, could have very well been the low serum potassium.

Dr. L. Feldman:** When the electrocardiogram was taken, the serum potassium level was below normal. In hypopotassemia you may get negative or small T waves, ST segment depression, or a prolonged QT interval. The T waves may become flat or negative in counterdistinction to hyperpotassemia where you get elevated T waves. I may say from a clinical viewpoint, looking back at it now, that this electrocardiogram

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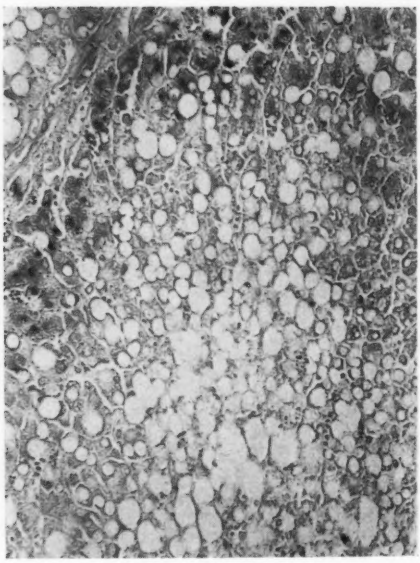

Figure 4

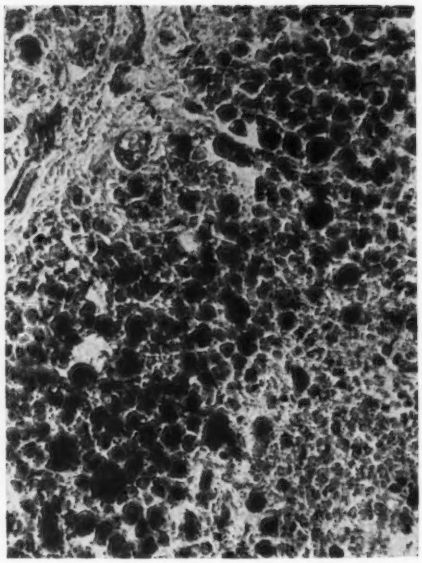

Figure 5

Liver. Portal Cirrhosis. Area of advanced fatty metamorphosis. Figure 4—H. E. 250X. Figure 5—Oil Red O, 200X.

fits into the clinical classification of hypopotassemia which the laboratory reported.

Dr. M. Kirshen:* If this patient's diarrhea had been the result of antibiotic therapy, such as the tetracyclines, there may have developed at one point a negative test for urinary urobilinogen. This situation would have been the result of sterilization of the gastrointestinal tract with the elimination of the normal bacterial flora which converts the bilirubin to urobilinogen. The net result would be the findings of obstructive jaundice, as indicated by a high direct serum bilirubin, elevated levels of urinary bilirubin and a negative urinary urobilinogen. Paradoxically, this would be contrasted with other liver profile tests which would indicate extensive hepatocellular damage which occurs in cases mind whenever a jaundiced patient is of obstructice jaundice only when the obstruction has been present six months or more. These facts should be kept in given antibiotics that can sterilize the gastrointestinal tract.

Dr. S. Zakon:** The late Dr. Otto Stein of Vienna was a doctor in a prison camp and he made careful observations on the effect of starvation on the prisoners. He described a syndrome of gynecomastia, atrophy of the testicles, and spider nevi in these malnourished people. The other remark I would like to make is that the history states that this patient was a heavy drinker, consuming about one-half pint of brandy a day. Thus he probably could not afford an adequate balanced diet.

Dr. H. Rappaport:* As may be expected from the clinical discussion, the principal pathologic alteration was found

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in the liver. The liver was very much enlarged, weighing 3,000 grams. It was firm in consistency but the surface was fairly smooth and did not present the nodular appearance which one might expect in an advanced stage of portal cirrhosis. However, close examination of the cut surface disclosed considerable distortion of the normal architectural pattern. The color was deep yellowish-brown and individual liver lobules did not have the appearance of normal lobules, but of small regenerates.

The microscopic picture of the liver was particularly striking. The normal lobular architecture was completely distorted by the presence of atypical parenchymal regenerates which were separated by branching connective tissue bands of varying width (Fig. 1). The usual regular relationship between portal triads and central veins was absent. In many areas the parenchymal cells showed an advanced stage of necrobiosis (Fig. 2).

Frequently, necrotic cells were diffusely stained with bile pigment. In many of the liver cells the cytoplasm was heavily clumped, and in some of them it contained deeply acidophilic hyaline-like bodies which resembled the acidophilic bodies described by Mallory[1] in alcoholic cirrhosis. In some areas where the parenchymal cells were preserved, the intra-lobular bile canaliculi were plugged with inspissated bile, so-called bile thrombi, particularly in the periphery of the lobules (Fig. 3).

This type of retention may be due to the fact that in the course of the development of the parenchymal regenerates, extra and intra-lobular bile ducts fail to connect. In addition, massive destruction of liver cells interferes with the intra-lobular flow of bile. A moderate degree of bile duct proliferation was present in the connective tissue septa.

Another striking feature was a severe degree of fatty metamorphosis with the cytoplasm of many of the cells almost completely replaced by fat droplets (Figs. 4 and 5). The fatty metamorphosis probably accounted for the greater part of the liver enlargement.

Many of the parenchymal cells contained increased amounts of iron as demonstrated by the Prussian blue reaction. The hemosiderin was more prominent in the parenchymal than in the Kupffer cells. There was a remarkable paucity of inflammatory changes, indicating both the recent nature of the necrobiotic changes as well as the absence of a true hepatitis. Only a few small focal aggregates of polymorphonuclear and mononuclear leucocytes were seen in the perilobular connective tissue.

We interpret the findings in the liver as indicative of portal (dietary) cirrhosis, with acute necrobiosis of liver cells. The term "florid cirrhosis" was applied to this entity by Popper and associates.[2] It is believed that inter-current infections in patients with severe metamorphosis and/or cirrhosis may impair liver function to such an extent that hepatic insufficiency ensues.

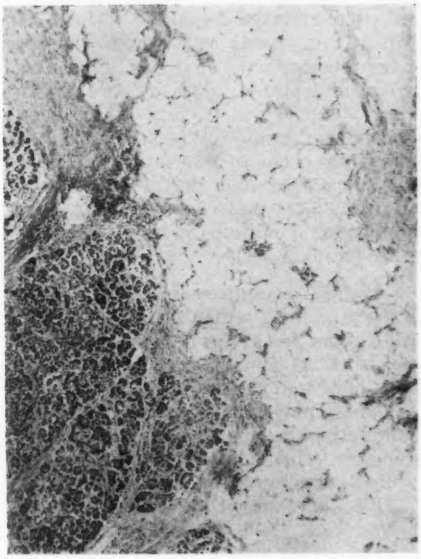

Figure 6

Pancreas. Fatty infiltration and fibrosis. H. E. 65X.

[1]Mallory, F.B. Cirrhosis of The Liver. NEJM, *206:* 1231-39, 1932

Figure 7
Pancreas. Medium sized excretory duct containing inspissated secretions. H. E. 80X.

The relation of fatty metamorphosis to nutritional deficiency does not require any further amplification. However, the presence of large amounts of hemosiderin in the hepatic cells when occurring in conjunction with cirrhosis is frequently misinterpreted as hemochromatosis. This is not correct since it has been shown that hemosiderosis does not infrequently occur in association with fatty metamorphosis and portal cirrhosis of the liver. The cause of the hemosiderosis in these conditions is not as yet clearly understood.

I would like to discuss now certain laboratory findings which are of interest in this connection. The hematological findings such as macrocytic anemia with a high color index, many reticulocytes, target cells, polychromatophilia and basophilic stippling are quite consistent with anemia of chronic liver insufficiency. It is unfortunate that no studies were done to rule out hemolytic anemia.

Impairment of liver function is also reflected in a prothrombin time of 19 seconds and clotting activity of only fifty per cent. Of great interest are the elevated alkaline phosphate level and the fact that of the total bilirubin of 24.4 mg/100 cc., the direct bilirubin represented the major portion (15.2 mg/100 cc.). These laboratory data suggest that an obstructive mechanism contributed to the jaundice to a considerable degree. On the other hand, the total serum cholesterol of 208 with only 14 per cent esters is indicative of severe hepato-celluiar damage.

In our case, the microscopic sections of the liver show that the jaundice was the result of both — the destruction of liver cells and intra-lobular bile stasis, the mechanism of which has already been discussed. This point is frequently forgotten in the differential diagnosis of jaundice, namely, that the direct bilirubin may be increased not only due to obstruction of the extra-hepatic bile ducts but also to obstruction of the intralobular bile canaliculi. Lack of increased urobilinogen excretion in the urine in

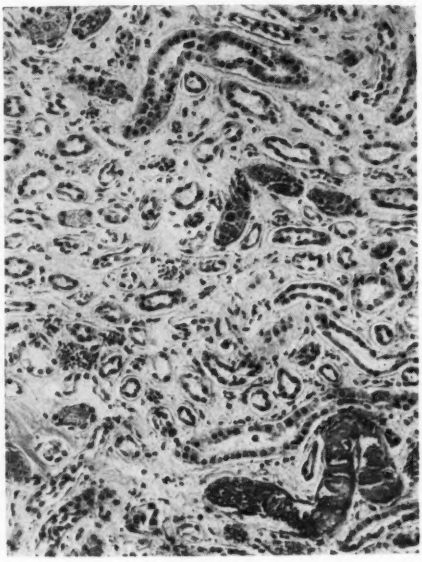

Figure 8
Kidney. Chlomic nephrosis. Note bile casts within tubules. H. E. 220X.

[2]Popper, H., Szanto, P.B., and Parthasarathy, M. Florrid Cirrhosis. A Review of 35 Cases. Am. J. Clin. Path., 25: 889-902, 1955

the presence of such severe liver cell destruction may also be explained by a cholesterol of 208 with only fourteen per cent esters is indicative of severe hepatocellular damage.

In addition to the liver, interesting pathologic alternations were found in other organs also. Both lungs were voluminous, one weighing 800 grams and the other, 900 grams. In both lower lobes there was confluent bronchopneumonia. While the pneumonia did not appear to be particularly recent, it is impossible to establish on the basis of the postmortem findings whether or not it was present at the time of the patient's admission and whether or not it could account for the high white cell count. We found no other infection to account for it and we believe that the extensive liver necrosis at necropsy occurred rather late in the course of the patient's illness.

Severe fatty infiltration was found in the myocardium and the pancreas (Fig. 6), the latter organ showing, in addition, extensive fibrosis and inspissated secretions in some of the medium sized ducts. (Fig. 7) Occasional focal areas of pancreatic fat necrosis were present.

The kidneys were markedly enlarged. Each weighed 240 grams and showed what we would expect to see in a patient with severe jaundice, namely, so-called cholemic nephrosis. Many of the renal tubules, particularly in the excretory portion of the nephron, were filled with inspissated bile without much destruction of the parenchymal cells. (Fig. 8).

The adrenals showed focal areas of recent necrosis as well as old foci of calcification. While necrosis of the pancreas and cholemic nephrosis are not infrequently seen in this type of liver disease, the changes observed in the adrenals are distinctly unusual.

The patient also showed erythroid hyperplasia of the bone marrow which is entirely consistent with macrocytic anemia of liver insufficiency.

The spleen weighed 350 grams and showed acute splenitis which may be related to both the severe hepatic necrosis and the patient's bronchopneumonia.

Final Anatomical Diagnoses

1. Portal cirrhosis of liver with fatty metamorphosis and acute necrosis ("florid cirrhosis")
2. Hemosiderosis of liver
3. Bronchopneumonia, lower lobes
4. Fat replacement and fibrosis, head of pancreas
5. Fat infiltration of myocardium
6. Acute focal necrosis of adrenals
7. Focal calcifications of adrenals
8. Cholemic nehprosis
9. Erythroid hyperplasia of bone marrow
10. Cholelithiasis

BOOK REVIEWS

CHRISTOPHER'S TEXTBOOK OF SURGERY. Edited by Loyal Davis, M.D. Sixth Edition. 1484 pages, with 1359 illustrations on 716 figures. Philadelphia: W. B. Saunders Company, 1956. $15.50.

Medical scholars who have long awaited the promised revision of Christopher's Textbook of Surgery, were finally rewarded for their patience in February with the appearance of this American classic. Under the able direction and editorial scrutiny of Dr. Loyal Davis of Northwestern University, this book has been thoroughly re-written and brought up to date.

Although each chapter is individually written by a specialist in the particular field, there is a remarkable continuity between the various subjects which makes the book extremely readable. In this respect, the novel but short biography which introduces each author, undoubtedly aids in achieving this effect. The large, dark type on glossy stock, the double column page, contribute also to easy reading. Diagrams, photographs, charts and tables, introduced strategically in the discussion, aid in understanding without confusing the reader.

The subject of general surgery is divided into thirty-four chapters on a regional basis. Included also are special chapters on gynecological and urological problems which form short but extreme helpful reviews of these specialties that may be of special interest to the general practitioner and surgeon.

It is Dr. Davies' interest to present a philosophy of surgery based upon sound physiological fact rather than the mechanics and techniques of surgical practice. But this does not prevent him from describing in detail numerous, simple routine procedures which are expected to be performed by an intern on any surgical service. Pathogenesis, diagnosis, and differential diagnosis are treated adequately as would be expected of a text of this calibre. Management has been brought up to date, with references from 1955 being included in the bibliography at the end of each chapter.

It is this reviewer's opinion that the chapters on diseases of the breast, the stomach, hernia and intestinal obstruction are amongst the best. Each deals with a subject that is both important and confusing to the student. However, frank, lucid discussions based on pathology, physiology and pathogenesis clear the air of ambiguity to leave the reader with basic concepts and a feeling of understanding. It is noteworthy that the problem of gastric and duodenal ulcer is approached from the view points of both the internist and the surgeon, with the management of such a patient correlated to the benefit of the student and, of course, the patient.

Perhaps the poorest is that chapter on the thryoid, and this is principally due to Dr. Cril's (the co-author) interest in radioactive iodine as a therapeutic agent. Inclusion of material on the pre and post-operative management of the patient with disease of the thyroid would have made this an excellent chapter.

Needless to say, this new edition of Christopher's Textbook of Surgery is a "must" for every student and practitioner of medicine. Dr. Davies and the Saunders Company are to be congratulated for the magnificant task they have performed in revising this textbook.

* * * * *

DISEASES OF THE CHEST by H. Corwin Hinshaw, M.D., Ph.D., and L. Henry Garland, M.B., B.Ch. Cloth. First Edition. 727 pages. Philadelphia: W. B. Saunders Company, 1956. $15.00.

This surprisingly up-to-date textbook on diseases of the chest is a welcome addition to the medical literature. It is quite complete in material coverage, and therefore necessarily not as comprehensive on some subjects as might be desired. The authors should be complimented on their segmental approach to the clinical study of chest diseases, which has been lacking in most textbooks of chest diseases.

The importance of bronchoscopy from both a diagnostic and therapeutic standpoint is brought to the attention of the reader. Pulmonary function is adequately covered, but perhaps more from a didactic view than from its utilization in patients. Some of the finer points in early diagnosis of bronchiogenic carcinoma is ably presented. Diagnosis from both clinical and laboratory methods is quite complete. Therapeutic regimens recommended are up-to-date and well accepted amongst specialists in the field.

One of the most valuable aspects of this book, however, is its fine presentation of x-ray diagnosis of the disease entities covered carefully, indicating the value and limitations of the roentgenogram. It is profusely illlustrated with well selected x-ray findings which serves to augment the excellent text.

In view of the fact that this book is, to a large extent, aimed at the medical student, it perhaps should have gone into somewhat more detail in the art of physical diagnosis in chest diseases, which is so sorely losing its importance in present-day medical education. It might have lent somewhat to the understanding of disease processess if more space could have been relegated to the natural history of the disease entity and the physiology of the manifested symptoms.

This book is well indexed and has been made both easy and interesting to read. It is one of the finest books on the subject that has been published, and will be of great value to both student and practitioner.

Gerschen L. Schaefer, M.D.

PATHOLOGIC PHYSIOLOGY. Edited by William A. Sodeman, M.D. Cloth. Second Edition. 963 pages. Philadelphia: B. B. Saunders Company, 1956. $13.00.

The second edition of Pathologic Physiology promises to have as much success among students, interns and practitioners as the first. The book discusses diseases in the field of internal medicine in respect to disturbances in function. In particular, the author discusses symptoms as indicators of disturbances in the homeostatic mechanisms of the body. This book attempts to bridge the gap between textbooks of physiology and textbooks of cinical medicine, although it is in no way a substitute for either.

The reader often wishes that certain chapters had been expanded into more detail. The particular chapters concerned with genetics, growth and neoplasia, and physical, toxic and chemical agents fall into this category. Chapters devoted to the circulatory, respiratory and digestive systems are worthy of particular merit.

With the knowledge in mind of the essential deficiencies a book of this kind must entail, this work is worthy of consideration for the well-rounded library of the senior medical student, intern, resident or internist. It contains numerous outlines and functional drawings which will be found useful in categorizing many diverse disease entities and syndromes.

S.F.

* * * * *

COUNSELING IN MEDICAL GENETICS by Sheldon C. Reed. Cloth. First Edition. 268 pages. Philadelphia: W. B. Saunders Company, 1955.

The director of the Human Genetics Institute of the University of Minnesota has written this book to help the physician answer his patients' questions concerning heredity. Providing the patient limits himself to twenty questions, this book may be of use.

Dr. Reed discusses the twenty most common problems of congenital abnormalities that his clinic is consulted upon. They range from schizophrenia to skin color. A brief discussion of each entity is followed by statistical evidence of its hereditary basis. The author then gives the odds for a couple with this particular trait of passing it on to their children. The statistics are of small samples and dubious nature, however.

The most valuable part of this book is the presentation of probabilities of a congenital abnormality appearing in a second child after it has appeared in a first, something which every doctor would like to know in counseling patients who have had a misfortune of this nature.

Whether or not the author is justified in calling allergies, schizophrenia and maniac-depressive psychosis inheritable traits is open to question, however.

In summary, this book, despite its shortcomings, does contribute positively to the literature of a much disputed subject.

B.R.

A MODERN PILGRIM'S PROGRESS FOR DIABETICS by Garfield G. Duncan, M.D., Cloth. First Edition. 222 pages. Philadelphia: W. B. Saunders Company, 1956. $2.50.

This book is an endeavor, on the part of an outstanding authority in the field, to present to the lay public an awareness of the "ups and downs" in the life of a diabetic. The facts are presented in story form in order to make the situations real and personal.

At the end of the narrative, there is an excellent appendix which deals with diets, ideal weights, types of insulin and many other useful details. Dr. Duncan's efforts should do much toward enlightening the diabetic and his family about his disease.

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THE RELIEF OF SYMPTOMS by Walter Modell, M.D., F.A.C.P. Cloth. First Edition. 450 pages. Philadelphia: W. B. Saunders Company, 1955.

This book, intended primarily for medical students, is not, or does it pretend to be, a comprehensive textbook of pharmacology. Rather, it is what its title implies, a practical approach to the relief of what is most important to the patient—namely, his symptoms.

In this work, in addition to discussions on placebos, the masking action of the steroids, statistical evaluation of drugs, and the relief of the 24 symptoms which comprise the majority of presenting complaints, are treated at length. This book is very well organized in that it has a table of contents at the beginning and a summary at the conclusion of each chapter, as well as numerous charts for comparison of various drugs.

This work is highly recommended, with the proviso that it is used within its scope and not for the means of treating the symptoms while glossing over the underlying cause.

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CURRENT THERAPY, 1956. Edited by Howard F. Conn, M.D. Cloth. 632 pages. Philadelphia: W. B. Saunders Company, 1956. $11.00.

This is the eighth in a yearly series of methods of therapy of the common diseases met in medical practie, as presented by a group of authorities in their various fields.

The bock is subdivided into disease entities, a factor which is almost unavoidable in textbooks. However, this has its weakness in the sense that no case is absolutely similar to another, so that physicians, although they can use a book like this as a good foundation must still improvise as they go along.

Nevertheless, the latest book in this series is as excellent as its previous editions and is important in apprising the medical profession, not only of the latest methods, but in reiterating the proven older procedures, upon both of which thorough treatment of the entire patient is based.

TEXTBOOK OF MEDICAL PHYSIOLOGY by Arthur C. Guyton, M.D. Cloth. First Edition. 1030 pages. Illustrated. Philadelphia: W. B. Saunders Company, 1956.

This book promises to fill the gap which has long existed in the teaching of physiology. It is intended primarily for medical students and does not attempt to cover physiology in all its intricate experimental aspects. Rather, it is a concise presentation of the important topics in physiology as they are applied toward a general knowledge of medicine, and in addition, contains illustrative sections on the pathologic physiology of the more important clinical entities connected with the basic physiologic facts under discussion.

Another advantage of this work is its one-man authorship, which results in equitable distribution of space among the various subjects, rather than the uneven tone often found in textbooks written by several collaborators. Of special note are the sections on the cardiac cycle and on electrolyte and water balance, due to the great clarity of their presentation.

This book is highly recommended to all those who want and need physiology presented within the scope of general medical knowledge.

OFFICE PROCEDURES by Paul Williamson, M.D. Cloth. 412 pages. Philadelphia and London: W. B. Saunders Company, 1955. $12.50.

This is an extremely readable and informative text which will be of great value to the young intern and general practitioner. The book is organized in fifteen sections, giving general office procedure of the various systems. Included are sections on Minor Surgery, Psychological testing, Anesthesia, Physiology, and Roentgenography. Each section contains numerous diagrams which are clear and concise and which adequately clarifies the text. Principles and techniques are discussed giving the rational for the various procedures.

The book is a result of a series of notes which the author has compiled, lifting material from other authors as well as from his own experiences. Only the most frequently used procedures are included, which has been determined by a survey of the author's own clinical records and the records of his colleagues. The material presented is extremely comprehensive, giving a well organized approach to the patient for the various procedures.

ABSTRACTS SECTION

KAPLAN, MORRIS A. (Asst. Prof. Med.), EHRICH, NORMAN J., and AARONSON, ABE L. (Asst. Prof. Med.). Hay Fever—A Review of the Literature of 1953-54. Tnnals of Surgery, *13*:594-626, 1954.

In this report, at a number of chemical, immunologic, and serologic studies are discussed which may offer some possibility of solving the question of the role of the various allergens found in pollens. Then the individual allergens or fractions found in pollen are completely studied in relationship to their biologic activity as compared to their chemical nature, their true nature can be assayed.

New methods for preparation and separation involve hemogeneous solvents, electrophoresis, paper chromatography, and ion-exchange resin fractionation. Homogeneity, purity and standardization utilize new methods which involve ultra-violet absorption, spectra curves, and gel diffusion techniques. Serologic studies for antibodies involve special techniques for complement fixation, coated red cells, and inhibition tests.

Some of the newer anti-histimines and the uses and dangers of steroids are also discussed.

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KAPLAN, M. A. (Asst. Prof. Med.), AARONSON, A. L. (Asst. Prof. Med.), HENDERSON, J. and GOLDIN, M. (Asst. in Microbiology). C. Reactive Protein Levels and Anti Streptolyson O. Titres in Bronchial Asthma. A Preliminary Report. Annals of Allergy, *13*:29-34, 1955.

Attempts to differentiate and classify types of bronchial asthma associated with infection or bacterial allergy have long posed a serious problem. The terms "intrinsic" and "extrinsic" have been used to describe types of bronchial asthma, but have recently been found to be undesirable to many allergists because no good practical method has been advanced to differentiate them.

Direct and indirect skins tests, as well as other serologic tests often prove useless, making the diagnosis of bacterial allergy difficult.

In this study, C.R.P. and A.S.O. determinations were made on 101 patients with bronchial asthma. The presence of C.R.P. in the serum of the asthmatic patient would seem to indicate the possibility of an infectious allergic process. It would appear from this study that in the presence of a history of recent upper respiratory infection with asthma, the increase in C.R.P. precipitate would indicate possible evidence of an allergic infectios process. However, the A.S.O. antibody seems to be so diversified that it does not lend itself as an accurate measure of infection in bronchial asthma.

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AARONSON, ABE L. (Asst. Prof. Med.), KAPLAN, MORRIS A. (Asst. Prof. Med.), GOLDIN, MILTON (Asst. in Microbiology), LIBRETT, ARNALDO, and GOLDMAN, BETTY. C. Reactive Protein in Bronchial Asthmatic Patients. 2) Further Evaluation. Annuals of Allergy, *13*:586-591, 1955.

The present report concerns itself with further observations in 314 patients with bronchial asthma, of which 103 were adults and 201 children up to the age of 14 years; in addition, a control group of 43 non-allergic children with recent upper respiratory infections were tested for the presence of C. reactive protein.

It was found that in asthmatic patients classified as "infectious," the occurrence of a recent upper respiratory infection frequently produces C.R.P. in the serum. The results of this survey also show that C.R.P. occurs about ten times more often in asthmatic patients with a recent upper respiratory infection than in those without it.

In non-allergic children with a recent infection of the upper respiratory tract, C.R.P. is not present in the blood serum.

* * * * *

PRESMAN, DAVID (Clin. Assoc. Prof.). Eleventh Intercostal Space Incision for Renal Surgery. Jour. Urology, Vol. 74, No. 5, November 1955.

A description of the eleventh intercostal space, extrapleural lumbar incision for renal surgery is presented. Experiences with this incision in 42 patients has demonstrated its advantages over the standard Mayo lumbar approach. The improved exposure of the upper pole of the kidney and the renal pedicle has converted a blind procedure into a visualizing one.

This incision is a simple one and requiers no additional operating time. The only possible complication is trauma to thepleura and this can be easily avoided if the posterior extension of the incision is carefully performed. Although this incision has been used on a relatively small number of cases, the excellent exposure which has been obtained warrants its further use to determine its value in renal surgery.

* * * * *

STERN, KURT, M.D. (Assoc. Prof. Path.), DAVIDSOHN, ISRAEL, M.D. (Prof. Pathology). Effect of Estrogen and Cortisone on Immune Hemoantibodies in Mice of Inbred Strains. Jour. Immun., Vol. 74, No. 6, June 1955.

Estrogen was found to enhance significantly the production of immune hemolysin for sheep red cells in C57BL mice, whereas in C3H mice a moderate inhibition of hemolysin titers was noted in estrogen-treated animals. Cortisone was much more effective in depressing antibody titers for sheep red cells in mice of strain C3H than in those of strain C57BL.

Normal, untreated C57BL females showed significantly higher hemolysin titers than did C57BL

males. On the other hand, no such difference was found in males and females of strain C3H. The implications of these findings were discussed in relation to the innate difference in immune response characterizing C57BL and C3H strains and in connection with the horomonal physiology of these strains.

* * * * *

DIAMOND, SEYMOUR, M.D. (Asst. in Neurology). The Use of Methamphetamine Hydrochloride in Stokes-Adams Disease. Ammer. Pract. Digest Treat., Vol. 6, No. 8, August 1955.

Two cases of Stokes-Adams disease following acute myocardial infarction were treated with methamphetamine hydrochloride by injection. In the first patient, a man in whom the syncope and convulsions occurred on the seventh hospital day in the absence of shock, 120 mg. seemed to bring about a cessation of the attacks. In the second patient, a woman in profound shock the day after an accute myocardial infarction, 300 mg. were injected over a 16-hour period, and seemed especially effective when given intravenously during cardiac standstill. Both patients recovered and showed no ill effects from the use of this sympathomimetic drug.

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STERN, K., M.D. (Assoc. Prof. of Path.), SPENCER, K., M.D., FARQUAR, M., M.D. Effect of Polyvinyl Pyrrolidone on Immune Response in Mice. Proc. Soc. Exp. Biol. Med., Vol. 89, 126-131, 1955.

Administration of PVP to mice was found capable of drepressing levels of immune hemolysin for sheep red cells. This effect varied with the strain of mice used, timing if injection of PVP, type of antigenic stimulation and molecular size of the PVP compound. Depression of hemolysin appeared to be correlated with the degree of splenomegaly, but not with the PVP concentration in serum, liver and spleen.

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MILLER, DONALD S., M.D. Ph.D. (Prof. of Orthopedics and Traumatic Surg.), LICHTMAN, WILLIAM F., M.D. Diabetic Neuropathic Arthropathy of Feet. A.M.A. Archives Surg., Vol. 70, April 1955.

Seventeen cases of diabetic neuropathic feet, found in a five-year survey, have been observed; three of these were cases in private practice.

Physiologic trauma and neuropathy associated with diabetes mellitus are basic factors in the occurrence of such arthropathies of the feet. With the associated neuropathy there are an accompanying anesthesia, paresthesia, loss of sensation in joints, loss of or diminished reflexes pupillary changes, and reduced vibratory and position sense.

Ulcers, tissue necrosis, or nutritional tissue changes do not usually occur concomitantly with the progression of the deformity but are more likely to occur later after the deformity has taken place. On the other hand, in several cases, pressure necrosis or ulcers and low-grade tissue infections did appear earlier, which can probably be explained on a nutritional-tissue basis. In such cases there was roentgenographic evidence of advanced bone atrophy and bone changes.

Roentgenologic surveys in all cases disclosed two main types of osseous changes: (1) the atrophic type with dissolution of joints, absorption of bone, and atrophy of the metatarsus and tarsus; (2) the hypertrophic type with local destruction but with overgrowth of bone, and calcification in and around the involved joints. The second type occurred more frequently in our series. Displacement of bone, either in a dorsal or planter direction, was not uncommon.

The associated problems in our series were not unusual but might have been expected in a group whose average age was 53.17. The complications were primarily hypertension and heart disease as well as obesity. There were in addition instances of glaucoma, rheumatoid arthritis, cancer, cellulitis, alcoholism and cirrhosis of the liver, syphilis, and gangrene.

In general, diabetic neuropathic arthropathies of the feet are grave, often leading to total disability, with reduction or even loss of gainful occupation. Treatment is empirical and conservative, and the prognosis must be guarded.

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TURNER, S. J. (Clin. Assoc. Prof. Gyne. and Oct.); LeVINE, L. (Clin. Inst. Gyne. and Obst); and ROTHMAN, A. Lupus Erythematosus and Pregnancy. Amer. Jour. of Obst. and Gyne., 70: 102-8, 1955.

In spite of the fact that lupus erythematosus occurs most frequently in women of childbearing age, very few cases complicated by pregnancy have appeared in the literature to date.

One case of subacute disseminated lupus and another of acute disseminated lupus erythematosus complicated by pregnancy observed by the authors during the past two years were summarized and discussed.

The available data disclosed a 20 to 60 per cent maternal and 30 to 50 per cent fetal mortality in the acute and a 46 per cent fetal mortality in the subacute disseminated lupus erythematosus complicated by pregnancy. Patients with any form of lupus erythematosus may tolerate pregnancy well, provided the disease is under control and in a quiescent state. However, interruption of pregnancy may have to be considered in cases where the disease cannot be controlled medically.

ATCH and cortisone may be of value in controlling this disease.

* * * * *

SICKLEY, JEROME F., FRIEDMAN, IRVING A. (Clin. Inst. Med.), FELDHAHE, CHARLOTTE, and SCHWARTZ, STEVE O. (Prof. Hematology). In Vivo Demonstration of the Lupus Erythematosus Phenomenon. J. Lab. and Clin. Med., 46:624-627, 1955.

A method for the demonstration of the lupus erythematosus phenomenon in vivo, by use of a

constricting band around a digit is described. This method was applied to 23 cases of known lupus erythematosus and the results were found to be positive in 18. Fifty control patients gave negative results.

* * * * *

FOA, P. P. (Prof. Physiology and Pharmacology), GALANSINO, G., COSTA, E., and WEINSTEIN, H. R. Prolactin and the Secretion of Insulin and Glucagon by the Pancreas. Amer. Jour. Physiol., 182-493, 1955.

Eighteen cross-circulation experiments were performed by anastomosing the pancreatic-duodenal or a mesenteric vein of a donor *dog D* with a femoral vein of a recipient *dog R*. The intravenous injection of prolactin into previously untreated normal donors causes a lowering of the blood sugar in *dog D*, accompanied by liberation of insulin and consequent hypogyycemia in *dog R*. Prolactin causes hyperglycemia in donor dogs previously treated with repeated injections of this hormone. The blood sugar of *dog R* remains unchanged. The results indicate that the so-called diabetogenic effect of prolactin may be the result of a rapid dumping of preformed insulin by the B-cells of the islets of Langerhans, followed by decreased production. The avilable evidence suggests that prolactin does not cause an increase in glucagon secretion.

* * * * *

SCHWARTZ, STEVE O. (Prof. Hematology), SCHOOLMAN, H. M. and SUPRRIER, M. T. Studies in Leukemia. 3 Agglutination of Human Leukemic Cells by Guinea Pig Serum. J. Lab. and Clin. Med., *46*:709-712, 1955.

Agglutination tests of human leukemic white cells and human nonleukemic white cells with normal guinea pig serum were performed. Agglutination of the leukemic white cells but not nonleukemic white cells is described. In 423 cases, of which 56 were cases of leukemia, there were 4 false negative and 3 false positive recations. All false positives were in patients with advanced tuberculosis.

Of possible effects of various drugs employed, only cortisone was found to have an effect, and this was inhibitory.

It is proposed that this test may prove valuable in the diagnosis of aleukemic leukemias and in differentiating leukemoid reactions.

* * * * *

SCHARTWZ, STEVE O. (Prof. Hematology), and HARTZ, WILSON H. Mediterranean Anemia in the Negro. A Re-evaluation of Four Patients and Their Families. Blood. *10*:1256-1266, 1955.

Four Negro patients and their families previously reported in 1949 as examples of Mediterranean anemia, were re-evaluated with regard to hemoglobin concentration. Mediterranean anemia was confirmed in one entire family and in the index case of another family. Two entire families and one member of another family were found to possess hemoglobin C.

Although, in retrospect, it is found that those with hemoglobin C disease were found never to have jaundice or roentgenologic evidence of bone changes and less poikilocytosis and hypochromia, hemoglobin analyses are essential to establish the exact hemoglobin defect. Mediterranean anemia shows high levels of F hemoglobin, whereas hemoglobin C disease shows no significant change of the F fraction.

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SCHWARTZ, STEVE O. (Prof. Hematology). Hypersplenism. Indust. Med. and Surg. *24*:359-362, 1955.

This review discusses the diagnosis, therapy, and mode of action of "hypersplenism," a group of conditions characterized by various cytopenias, splenomegaly, and qualitatively and quantitatively adequate normal marrow. Seven cases, illustrating the condition in chronic lymphocytic leukemia, Felty's syndrome, Hodgkin's disease, acquired hemolytic anemia, Gauche's disease, and as a primary condition, are presented.

The normal spleen may be thought of as producing a hormone which regulated normal maturation and release of cells from marrow, and as removing effete cells. Possible explanations of hypersplensim are:

1) increased or abnormal effect, the spleen acting as an inhibitor or normal cell maturation and release from marrow;

2) sequestration of formed elements during circulation in the spleen;

3) formation by the spleen of abnormal cell lysins or agglutinins; or,

4) elaboration by the spleen of a reticuloendothelial stimulating substance, which, in turn, leads to either phagocytosis of cells, or liberation of agglutinating or lytic substances.

Treatment is splenectomy.

* * * * *

DOLAZ, E. J., DOLEHIDE, R. A. and FRIEDMAN, I. A. (Clin. Inst. Med.). Fibrinolysis in Patients with Metatactic Carcinoma of the Prostate Gland. Illinois Med Jor., *107*:110, 1955.

A case of metastactic carcinoma of the prostate with hemorrhagic diathesis secondary to circulating fibrinolysin is reported. Therapy with stilbesterol caused the fibrinolysin to disappear from the blood with subsequent correction of the bleeding time to normal, a negative fibrinolysin test, and improvement of the prothrombin time and prothrombin consumption, so that they approximate normal. The physiologic actions of prostatic enzyme and fibrinolysin with its effects are reviewed.

* * * * *

SKILLMAN, R. K. and FRIEDMAN, I. A. (Clin Inst. Med.). Afibrinogenemia in Pregnancy. Illinois Med. Jour., *106*:329-332, 1954.

A case of uterine and gingival bleeding due to afibrinogenemia in a pregnant Negro female

is presented. The mechanism in this case was assumed to be that of fibrinogen destruction from proteolytic activity. Of interest in the patient reported, was the presence of thrombopenia, also explained by a proteolytic process. The simple, practical means of diagnosis was emphasized, so that prompt specic therapy may be instituted early. The patient survived and had no further manifestations of afibrinogenemia.

* * * * *

SKILLMAN, R. K., SPURRIER, W., FRIEDMAN, I. A. (Clin. Inst. Med.), and SCHWARTZ, S. O. (Prof. Hematology). Rheumatic Fever Activity Determination by Two Correlative Methods. A.M.A. Archives of Internal Med., *96*:51-60, 1955.

The principle of antigen-antibody recation has been the basis for numerous tests to identify infectious diseases. It has also been shown that erythrocytes which have been coated with an antigen are agglutinated when antiserum prepared from this coating antigen is added. When complement is added to this system, under certain conditions, hemolysis occurs. Because rheumatic fever is associated with tissue reaction to Group A beta-hemolytic, it was the purpose of this study to determine whether a means of idnetifying a specific bacterial antigen, or antibodies elicited by it could be the means of ascertaining rheumatic fever activity.

Two methods of determination were employed: In one method, serum of rheumatic fever patients was used as antibody source; ase the antigen source, sheep red cells, coated with heat-killed Group A beta hemolytic streptococci, which had been isolated fro mactive rheumatic fever patients, were used; complement was added to produce hemolysis.

The other method utilized, as the antibody source, Group A. beta-hemolytic Streptococcus antiserum obtained from rabbits; for the antigen source reythrocytes of rheumatic fever patients, exposed to the antigen for coating in vivo, were used in an agglutination test.

In most instances the hemolysis method using patient's serum as the antigen source, was found to be somewhat more sensitive; in both metholds, treating erythrocytes with popain was found to enhance the reaction.

Control studies of seventy-seven varied patients including those from which alpha and beta-hemolytic streptococci were isolated, showed no instances in which other disease processes interfered with either test method. This would indicate an excellent sepcifity of these tests in active rheumatic fever.

Clinical correlations were obtained for sventy-eight rheumatic fever patients, most of whom were tested at intervals of the disease process. The titers in both these test methods were elevated within the rst few days of the active process in most cases, and they then gradually subsided and disappeared as the process became inactive. The results also indicated an excellent correlation between the test results and the clinical status of the disease, although the height of the titer was not indicative of the severity of the process.

It is concluded that these methods are of practical value is ascertaining activity or quiescence of a rheumatic process, as well in distinguishing rheumatic fever from other disease processes with similar clinical manifestations.

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